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CHOLINESTERASE ACTIVITY OF HUMAN SKIN

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It has been suggested that derangements of acetylcholine metabolism in skin may underlie the changes occurring in certain dermatoses. In view of this, more knowledge is needed both of the reactions of skin to acetylcholine and of the enzyme systems concerned in its metabolism in this tissue.

The presence of cholinesterase in skin was first demonstrated conclusively by Thompson and Whittaker (1944) and by Zeller, Kocher and Maritz (1944). The former authors, working chiefly with the rat, included two assays on human skin. Ord and Thompson (1950) next showed that activity in rat skin is mainly due to a "non-specific" or pseudo-cholinesterase. Hellmann (1952), using a histochemical technique, reported cholinesterase activity in the sweat glands of the pads of the cat's paw, also chiefly of the "non-specific" type; after sympathectomy this activity disappeared. In skin biopsies of the human axilla, however, Hurley, Shelley and Koelle (1953), also using a histochemical method, found only specific or "true" cholinesterase; this was located in the nerve endings to the eccrine sweat glands. They could not detect either type of cholinesterase in other structures in the skin except to a small extent in the blood vessels.

In view of these different findings in different species it was decided to undertake a more detailed survey of these enzymes in normal human skin. Because of the limitations of histochemical procedures, we have assayed enzyme activity manometrically using acetyl- β -methylcholine and butyrylcholine as substrates for true and pseudo-cholinesterase respectively. We have also used acetylcholine as substrate, which is hydrolysed by both types of esterase. A few

experiments have been carried out with separated dermis and epidermis, with tributyrin as substrate for the demonstration of aliphatic esterase, and with certain inhibitors.

Cholinesterase assays have also been made on skin specimens taken by biopsy from a few patients suffering from various dermatoses, including two cases of urticaria of nervous origin (reflex or cholinogenic) of the type studied by Grant, Pearson and Comeau (1936).

EXPERIMENTAL.

Materials.—Fifty-four samples of normal skin taken from 15 different regions of the body have been studied; 31 samples were obtained from males and 23 from females. Thirty-six specimens were obtained either by biopsy under local anaesthesia (from healthy subjects) or from surgical operations under general anaesthesia, and 18 post mortem. Skin cleansing agents used at biopsy or surgical operation are listed in Tables I and II.

In order to avoid senile skin changes, we have for the most part limited our studies to subjects not over 70 years of age.

Skin biopsies were taken from the forearm and scapular regions in 2 cases of reflex urticaria (men aged 22 and 31 respectively), and from 4 other conditions accompanied by whealing.

To prepare skin for assay the subcutaneous fat and connective tissue were scraped away, iodine or flavine used as antiseptics were wiped off as far as was possible, and the specimen rapidly minced with sharp scissors into a fine pulp. Enzymic assay was generally carried out immediately, but occasionally delayed for not more than 12 hours, the skin being kept refrigerated.

Methods.—Esterase activity on various substrates was estimated on weighed amounts of minced skin (usually about 150 mg.) at 38° C. and at pH 7.4. The free acid released from the choline ester by the action of the cholinesterase liberates carbon dioxide from the bicarbonate medium; the volume of CO₂ set free is then measured using the Warburg technique as modified by Ammon (1933). Measurements were done in duplicate, and corrected for non-enzymic hydrolysis of the substrate. Inhibitors, when used, were mixed with the minced skin in the Warburg vessel 20 minutes before the substrate was added. Activity is expressed as $\mu\text{l. CO}_2/\text{g. skin (wet wt.)}/\text{hr.}$

Dermis and epidermis were separated by means of tension applied longitudinally to skin strips (Van Scott, 1952).

Substrates.—0.015 M acetylcholine chloride or perchlorate (ACh), 0.03 M butyrylcholine perchlorate (BuCh) and 0.03 M acetyl- β -methylcholine chloride (MCh) were each dissolved in 0.025 M sodium bicarbonate immediately before use.

Tributyrin (TB) 0.03 ml. per flask was pipetted directly into the side-arm of the Warburg vessel.

RESULTS.

Normal skin.—The levels of true and pseudo-cholinesterase in normal skin, obtained either by biopsy or at surgical operation in males and females, are shown in Tables I and II respectively.

TABLE I.—*Cholinesterase Activity of Normal Skin obtained at Surgical Operation from Male Patients.*

(Activity expressed as $\mu\text{l. CO}_2/\text{g./hr.}$)

Region.	Skin antiseptic.	Age of subject.	ACh.	BuCh.	MCh.	BuCh/ACh.
Anterior abdominal wall . . .	Iodine .	61 .	274 .	721 .	134 .	2.6
" " " . . .	" .	33 .	437 .	756 .	113 .	1.7
" " " . . .	CTAB .	58 .	311 .	682 .	— .	2.2
" " " . . .	Dettol .	47 .	377 .	614 .	— .	1.6
Loin	Ethanol .	51 .	563 .	836 .	180 .	1.5
Interscapular	Iodine .	24 .	272 .	657 .	55 .	2.4
Forearm	CTAB .	32 .	577 .	799 .	— .	1.4*
" " "	" .	41 .	— .	723 .	— .	—*
Inguinal	Iodine .	49 .	431 .	664 .	93 .	1.5
" " "	" .	44 .	564 .	959 .	163 .	1.7
" " "	" .	63 .	297 .	628 .	— .	2.1
" " "	Ethanol .	18 .	580 .	977 .	206 .	1.7
" " "	Iodine .	62 .	581 .	1015 .	104 .	1.7
" " "	Flavine .	65 .	470 .	1024 .	— .	2.2
" " "	Iodine .	37 .	276 .	— .	— .	—
Finger (volar)	" .	48 .	590 .	900 .	— .	1.5
" (dorsal)	" .	48 .	412 .	546 .	— .	1.3
Scrotum	" .	38 .	510 .	— .	— .	—
Chest (anterior)	CTAB .	32 .	— .	603 .	— .	—*
Means			442	770	131	1.8
S.E. of mean			± 30	± 38	± 18	

* Biopsies taken under local anaesthesia.

In the 17 male samples studied with acetylcholine as substrate, cholinesterase activity ranged from 272–590 $\mu\text{l.CO}_2/\text{g./hr.}$ with a mean of 442; the 13 female samples showed activities in the presence of acetylcholine ranging from 285–842 $\mu\text{l.CO}_2/\text{g./hr.}$, with a mean of 592.

However, Tables I and II show that butyrylcholine is hydrolysed by human skin nearly twice as rapidly as acetylcholine; the mean BuCh/ACh ratios for the male and female samples being 1.8 and 1.9 respectively. Acetyl- β -methylcholine, on the other hand, is hydrolysed relatively slowly. These findings strongly suggest that a pseudo-cholinesterase is responsible for most of the hydrolysis of acetylcholine.

The higher activity in female skin as compared with male, with acetylcholine as substrate, is even more marked with butyrylcholine. Thus, while the 17 values in the male average 770 $\mu\text{l.CO}_2/\text{g./hr.}$, the mean value for the 16 specimens from females is 1148 $\mu\text{l.CO}_2/\text{g./hr.}$, and 12 of these specimens showed

TABLE II.—*Cholinesterase Activity of Normal Skin obtained at Surgical Operation from Female Patients.*(Activity expressed as $\mu\text{l.CO}_2/\text{g./hr.}$)

Region.	Skin antiseptic.	Age of subject.	ACh.	BuCh.	MCh.	BuCh/ACh.
Anterior abdominal wall	Ethanol	60	500	1058	91	2.1
" " "	Iodine	45	667	793	—	1.2
" " "	Flavine	49	628	825	—	1.3
" " "	"	26	—	1256	—	—
" " "	CTAB	52	842	1338	147	1.6
Chest (anterior)	Dettol	61	559	1435	56	2.6
" " "	"	53	485	1164	38	2.4
" " "	"	31	649	1346	53	2.1
" " "	Iodine	54	285	—	103	—
" " "	"	43	742	2064	—	2.8
" " "	"	46	777	1194	—	1.5
" " "	"	34	—	1196	—	—
" " "	CTAB	25	—	1141	—	—
" (side)	Iodine	45	346	655	71	1.9
Neck (anterior)	"	63	702	1045	196	1.5
" " "	"	31	520	714	—	1.4
Inguinal	"	35	—	1145	—	—
Means			592	1148	94	1.9
S.E. of means			± 45	± 84	± 19	

levels of activity greater than the highest rate given by any of the operation specimens from the males. The level of true cholinesterase, however, does not differ significantly in the two sexes.

Table III summarises the results obtained with specimens of normal skin taken post mortem. The mean values obtained in the male with acetylcholine and butyrylcholine are both lower than those obtained from biopsy or at operation, while in the female the mean rate of butyrylcholine hydrolysis is very considerably lower, being actually less than in the male. Individual values are moreover widely variable, the activity of one male specimen (from the anterior surface of the neck) being higher than that found in any of the operation specimens in the male. Yet the levels of true cholinesterase in the post-mortem specimens agree well with those found in the operation samples.

The lower levels of pseudo-cholinesterase in post-mortem skin were unexpected, as this enzyme loses little activity in other tissues on storing in the cold for 1–3 days. Bacterial multiplication on the skin surface and in the hair follicles (Lovell, 1945), or autolytic processes, might however be a factor, for in some cases 6–8 hours elapsed from the time of death until the body was refrigerated and up to 24 hours elapsed before the sample was removed from the body. Yet samples taken at surgical operations, in which immediate assay showed high cholinesterase levels, did not show a falling off in activity if kept for 4 days at 3°C. However, the majority of post-mortem subjects had died in hospital with diseases resulting in varying degrees of nutritional disturbance, the significance of which is discussed later.

TABLE III.—*Cholinesterase Activity of Normal Skin obtained Post Mortem.*

(Activity expressed as $\mu\text{l. CO}_2/\text{g./hr.}$)							
Region.	Age.	ACh.	BuCh.	MCh.	BuCh/ACh.	Cause of death.	
<i>Males :</i>							
Chest (anterior) .	70	688	874	212	1.4	Carcinoma bronchi.	
" " .	59	—	349	—	—	Congestive heart failure and sub-acute bacterial endocarditis.	
Lumbar (mid-line)	70	295	433	52	1.5	Carcinoma bronchi.	
Anterior abdominal wall	Still-born	—	695	—	—	Cerebral haemorrhage.	
Ditto	59	310	479	—	1.5	Multiple myeloma.	
" " .	59	—	466	—	—	" "	
Neck (anterior) .	59	—	549	—	—	" "	
" " .	21	—	1206	—	—	Electrocution.	
Axilla .	21	—	795	—	—	" "	
Upper arm (anterior)	59	—	477	—	—	Multiple myeloma.	
Hand (dorsum) .	39	389	709	62	1.8	Cerebral haemorrhage.	
Forearm (volar) .	59	445	477	—	1.1	Multiple myeloma.	
Means		425	626	109	1.5		
<i>Females :</i>							
Chest (anterior) .	63	788	1295	190	1.6	Carcinoma of larynx.	
Anterior abdominal wall	36	285	372	87	1.3	Cerebral haemorrhage.	
Ditto	68	328	575	81	1.8	Carcinoma of thyroid.	
" " .	63	302	345	82	1.1	" " larynx.	
" " .	52	348	430	81	1.2	Acute leukaemia.	
Forearm (volar) .	36	399	513	—	1.3	Cerebral haemorrhage.	
Means		408	588	104	1.4		

The cholinesterase activities (with butyrylcholine as substrate) of a number of different regions of the body are given in Table IV. Because of the generally lower activity in post-mortem skin and the presence of pre-existing disease, the results listed in Table IV are restricted to biopsy and operation specimens. Although the values for some areas represent only one specimen it will be seen that in the male the levels of activity fall within a relatively narrow range, but that in the female the scatter is somewhat wider. More assays from more areas are needed before conclusions as to regional variation can be reached.

We have limited our study to specimens from subjects not over the age of 70, and cholinesterase activity of the skin does not seem to change significantly up to this age. However, an operation specimen, not included in these Tables, from a man aged 75 gave very low values, namely 132 and 318 $\mu\text{l.CO}_2/\text{g./hr.}$ for hydrolysis of ACh and BuCh respectively; true cholinesterase activity however was within the usual range: 126 $\mu\text{l.CO}_2/\text{g./hr.}$ In addition, assays giving low values were done on an amputated leg from a female diabetic aged 77 with gangrene of the toe; but it is uncertain whether the skin from this subject can be considered normal, although clinically it appeared to be so.

TABLE IV.—*Mean Pseudo-cholinesterase Levels in Normal Skin from Different Body Regions obtained from Patients under the Age of 70 (Biopsy and Operation Specimens only).*

(Activity expressed as $\mu\text{l. CO}_2/\text{g./hr.}$)			
Region.	Male.		Female.
Anterior abdominal wall	693 (4)	.	1054 (5)
Chest (anterior)	603 (1)	.	1363 (7)
Chest (side)	—	.	655 (1)
Loin	836 (1)	.	—
Interscapular	567 (1)	.	—
Neck (anterior)	—	.	880 (2)
Inguinal	878 (6)	.	1145 (1)
Forearm (volar)	761 (2)	.	—
Finger (volar)	900 (1)	.	—
Finger (dorsal)	546 (1)	.	—

(Number in brackets = number of specimens.)

The various agents (iodine, surgical spirit, Dettol, flavine or cetrimide) used for cleansing the skin and the local anaesthetic (2% procaine 1–2 ml.) used for the skin biopsies do not appear to have had any inhibitory action. Procaine is not a powerful cholinesterase inhibitor (Bullock, 1948), and the injection probably lay largely in the loose subcutaneous tissues, the amount present in the true skin being very small.

Characterization of the Pseudo-cholinesterase of Skin.

A few experiments have been carried out to characterize more exactly the enzyme in normal skin responsible for the rapid hydrolysis of butyrylcholine.

Summation experiments with tributyrin and butyrylcholine indicate that these substrates are hydrolysed by different enzymes; thus, the rates of hydrolysis in one experiment were 575, 1160 and 1598 $\mu\text{l.CO}_2/\text{g./hr.}$ for BuCh, TB and BuCh + TB respectively, i.e. 92% "summation." Also 10^{-6} M eserine sulphate produced 75% inhibition of butyrylcholine hydrolysis but only 10% inhibition of tributyrin hydrolysis; with human brain Ord and Thompson (1952) reported corresponding inhibitions of 89% and 10% respectively. Lastly 2×10^{-9} M diisopropyl fluorophosphonate (DFP) produced 44% inhibition of BuCh hydrolysis, which agrees well with the I_{50} values of 2.6×10^{-9} M and 1.4×10^{-9} M found for pseudo-cholinesterase in human plasma and white matter respectively (Ord and Thompson, 1952).

Cholinesterase Activities of Separated Dermis and Epidermis.

We have also assayed activity in separated dermis and epidermis (samples being checked histologically), and in 4 experiments with BuCh the mean values for whole skin, dermis and epidermis were 1080, 740 and 80 $\mu\text{l.CO}_2/\text{g./hr.}$ respectively, expressed on a gram-weight basis for each tissue.

The pseudo-cholinesterase of normal human skin is therefore present in both epidermis and dermis but very largely situated in the latter. Hydrolysis of acetyl- β -methylcholine by epidermis was not measurable.

Cholinesterase Levels in Cholinogenic Urticaria.

The pseudo-cholinesterase levels in skin taken from 2 male subjects with cholinogenic urticaria were found to be 408 and 343 $\mu\text{l}.\text{CO}_2/\text{g}./\text{hr.}$ (BuCh as substrate) for specimens obtained from the scapular and forearm regions respectively. By comparison with the values found in normal skin (Table IV) it will be seen that these two values are considerably reduced. In a few cases of other conditions showing whealing which we have so far studied, namely idiopathic chronic urticaria, "pressure urticaria," dermatographia and urticaria pigmentosa, the cholinesterase levels have been normal.

DISCUSSION.

The results described above indicate that healthy human skin has a cholinesterase content such that 0.015 M acetylcholine is hydrolysed under our conditions at the rate of $442 \pm 30 \mu\text{l}.\text{CO}_2/\text{g}./\text{hr.}$ in the case of males, and $592 \pm 45 \mu\text{l}.\text{CO}_2/\text{g}./\text{hr.}$ for females. This agrees well with the earlier work of Thompson and Whittaker (1944). Both true and pseudo-cholinesterases are present, and the rate of hydrolysis of butyrylcholine very considerably exceeds that of acetyl- β -methylcholine. This conflicts with the histochemical findings of Hurley, Shelley and Koelle (1953) in human axillary skin, who found only weak pseudo-cholinesterase activity, situated in the blood vessels, much the greater activity apparently being due to true cholinesterase situated in the nerve endings to the eccrine sweat glands; moreover, neither enzyme could be demonstrated in the epidermis. In their studies, pseudo-cholinesterase activity on acetylthiocholine was presumed inhibited by 5×10^{-10} M DFP, a concentration which is considerably less than that used previously by Koelle (1951) for this purpose.

Although both male and female skin contain approximately the same level of true cholinesterase activity, pseudo-cholinesterase is present in significantly greater amounts in the female; thus, the mean value for male skin, with BuCh as substrate, is $770 \pm 38 \mu\text{l}.\text{CO}_2/\text{g}./\text{hr.}$, and for female skin $1148 \pm 84 \mu\text{l}.\text{CO}_2/\text{g}./\text{hr.}$ (differences between means = 378, $P = 0.001$). This higher activity in female skin has no obvious explanation, although differences in skin thickness might be the cause, in that a greater amount of non-cellular fibrous material in a given area of skin might be expected to reduce the activity found when expressed on a weight basis. If this were so, however, it might be expected that the level of true cholinesterase would also be higher in the female, but we have not found this to be so.

The greater pseudo-cholinesterase activity in the female might account for the finding that the female exhibits local sweating to acetylcholine introduced intradermally less readily than does the male (Kahn and Rothman, 1942; Gibson and Shelley, 1948; Janowitz and Grossmann, 1950), although this difference in response was not found by Chalmers and Keele (1952). Lewis (1945) reported that females exhibit whealing in response to doses of intradermal carbaminoyl choline which in the male cause only a flare. Whether this difference in response can be related to differences in cholinesterase levels is unknown; if any relationship exists male skin might indeed be expected to give the more vigorous response.

The results given in Table IV show no marked differences in activity in different regions of the body surface in the assays on male operation specimens, though in the female values are highest on the upper anterior trunk and lowest on the side of the trunk; here again differences in skin thickness must be taken into consideration as a possible cause. It would be of interest to correlate regional differences of cholinesterase activity with the regional distribution of thermal sweating reported by Kuno (1934) and Weiner (1945); however this cannot be done with our data. As pointed out above, a more extensive survey is required before conclusions can be reached, including assays on areas such as the palms, soles, cheeks and forehead. In addition, assays of skin from sympathectomized regions would be of great interest to compare with findings in the cat (Hellman, 1952).

The lower levels of activity we have found in skin obtained post mortem from hospital patients may well have been due to the general condition of these patients at the time of death. It is known that the plasma cholinesterase falls in liver disease (Antopol, Tuchman and Schifrin, 1937; McArdle, 1940), and that in malnutrition both the plasma cholinesterase (Hutchinson, McCance and Widdowson, 1951), and the liver pseudo-cholinesterase are lowered (Waterlow, 1950). In a skin specimen from a female, aged 42, who died as a result of a carcinoma of the breast with widespread metastases and jaundice, we found the very low level of $169 \mu\text{l.CO}_2/\text{g.}/\text{hr.}$ for pseudo-cholinesterase; in another case of diffuse carcinomatosis in a man aged 70 the skin of the front of the chest gave activity of only $158 \mu\text{l.CO}_2/\text{g.}/\text{hr.}$ with ACh as substrate.

Clinical Implications.

As our observations of cholinesterase in skin are clearly only a preliminary study, it is perhaps premature to attempt to relate them to clinical problems; it is difficult even to interpret them in the light of present knowledge of the physiology of the skin. Thus, the presence of acetylcholine in skin has not been demonstrated, the work of Rothman and Coon (1940) being inconclusive; the presence of cholinesterase in skin, however, is strong presumptive evidence

for the existence of cholinergic mechanisms in this tissue. Also, the behaviour of skin in the presence of cholinesterase inhibitors and of atropine suggests that such mechanisms are at work. For example, Skouby (1951) has shown that following the injection of prostigmine into the skin stimuli which are normally painless result in pain being felt, whereas a stimulus that is normally painful is no longer so if atropine is previously given intradermally. These observations were interpreted as indicating that changes in the concentration of active acetylcholine normally liberated in the skin influence the sensitivity of the nerve endings responsible for the perception of pain. Similar observations and conclusions were made by Bing and Skouby (1950) in regard to perception of cold. Further support to the view that cholinergic mechanisms occur in skin is provided by the work of Brown and Gray (1948), who have shown that injections of acetylcholine into the skin of cats and dogs cause a centripetal discharge of impulses in the nerves, presumably sensory, supplying the area injected. The large body of evidence showing that eccrine sweat glands respond to cholinergic drugs however does not prove that the normal metabolism of sweat glands involves acetylcholine, for pharmacological effects may not be identical with physiological actions.

We have seen nevertheless that there is evidence for the presence of acetylcholine or a similar substance in the skin, and that it may be related to the function of the sensory nerves. In this connection Emmelin and Feldberg (1947) have shown that histamine and acetylcholine pricked into the skin together lead to a burning sensation with prolonged itching, whereas histamine alone leads only to transient itching.

The physiological role of acetylcholine in the vascular reactions of the skin is another issue over which definite conclusions have not been reached from experimental work. Dale (1933) suggested that the flare of the triple response in skin is due to the release of acetylcholine from effector nerve endings of an axon reflex; that acetylcholine is involved has not been proved or disproved, and in addition vasodilator nerves have not been demonstrated in human skin. One interesting and suggestive piece of evidence however was presented by Lewis (1942) in his report of a case of cholinogenic urticaria. In this condition, in which urticaria is precipitated by heat, exercise and emotion, Grant *et al.* (1936) had concluded that the skin reacts abnormally to normal amounts of acetylcholine released at nerve endings. In Lewis's patient there was also an abnormal triple response to injury, for small delayed wheals appeared in the area of the flare, in addition to the usual wheal at the site of the stimulus. This was interpreted as being due to the highly abnormal way in which the skin of the patient reacted to acetylcholine released by the axon reflex in the area of the flare. Both flare and delayed wheals were inhibited by the prior injection of local anaesthetic. Hopkins, Kesten and Hazel (1938) reported a similar phenomenon in four patients with cholinogenic urticaria; outlying

wheals appeared in the area of flare produced by the intracutaneous injection of 0.01 mg. of mecholyl, and they suggested that wheals situated in the flare might be due to acetylcholine released by the axon reflex, although diffusion of mecholyl could not be ruled out.

If as a result of central stimulation excessive amounts of acetylcholine were liberated in the skin from cholinergic nerve endings, or if the skin cholinesterases were deficient in amount or were inhibited, the concentration of acetylcholine might rise to high levels, and one might expect the cutaneous nerves to respond to stimuli that would not normally excite them, or even that excitation would occur in the absence of the usual stimulus. A condition named "cholinogenic itching" has been described by Nomland (1944) wherein the patient suffers from intense pruritis, without urticaria, precipitated by emotion, heat and exertion. The itching is also, it is claimed, provoked by mecholyl. A similar case was described by Hopkins *et al.* (1938). This condition seems to be related to cholinogenic urticaria of (Grant *et al.*, 1936). Recently Cormia (1952), in studies of experimental itching produced by histamine, claimed that emotional disturbance results in itching being provoked by a smaller dose of histamine than that which is required normally by the subject in the absence of emotional stress.

Whether or not derangements of acetylcholine metabolism in the skin are associated with the pruritus and vascular changes which accompany many dermatoses is unknown; but one could postulate excessive liberation of acetylcholine in the skin, or reduced activity of cholinesterase due to deficiency of this enzyme or to the presence of inhibitors. Deficiency in skin cholinesterase was suggested by Peters and Silverman (1946) as one possible mechanism underlying cholinogenic urticaria. Morgan (1953) has recently reported three patients suffering from this condition in which the serum cholinesterase was low, but no values are given for the level in skin. In the two cases which we have studied the activity of pseudo-cholinesterase in the skin was reduced. If further work confirms this finding, a diminished cholinesterase activity in the skin of these patients may go a little way to explaining the mechanism of this disease; for, if the skin cholinesterase is reduced in activity, acetylcholine released normally in the skin might be expected to persist for a longer time and in a higher concentration than in the normal subject, and thereby induce the abnormal reaction of the skin in the manner suggested by Grant *et al.* It is not yet possible to say whether variations in the cholinergic mechanisms of the skin are of importance in other types of dermatoses, as claimed by Loewenthal (1949).

SUMMARY.

1. Values have been obtained for cholinesterase activity in 54 samples of normal human skin.

2. Both types of cholinesterase are present; pseudo-cholinesterase being in considerably greater amounts.
3. Pseudo-cholinesterase activity per unit weight of skin is greater in the female than in the male.
4. Pseudo-cholinesterase activity is present in dermis and epidermis, but is very much greater in the former.
5. Low levels of pseudo-cholinesterase have been found in two cases of cholinogenic urticaria.
6. Physiological and clinical implications are briefly discussed.

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SOME FURTHER OBSERVATIONS ON ALLERGIC CUTANEOUS ARTERIOLITIS.

M. RUITER.

Professor of Dermatology, State University, Groningen, The Netherlands.

IN previous papers (Ruiter, 1952, 1953) we have made an attempt to group together a number of skin disorders which were until then unsatisfactorily defined or not classified at all. They showed all the clinical picture of a haemato-genous disseminated eruption; the clinical course, the histopathological examination and the "allergic temperament" of the skin lesions suggested an allergic pathogenesis (drugs, micro-organisms, etc.); and the presence of focal infection and the history of allergy in the patient or his family in some cases were in accordance with this view. The histopathological changes demonstrated in these various eruptions were essentially the same although varying in detail in different cases. They consisted of inflammatory changes in the blood vessels, showing the histopathological picture of an allergic inflammation such as may be found, for example, in drug and infectious allergy. Particularly with regard to the evaluation of the clinical skin manifestations a distinction was made between disorders in which mainly the smaller (dermal) vessels were affected and those in which particularly the medium-sized (subcutaneous) vessels were involved (the cutaneous type of periarteritis nodosa). Particular attention was paid to the former group, which we described under the denomination "allergic cutaneous arteriolitis," and a number of clinical morphological characteristics found more or less regularly in this group were specified. Thus it became evident that in these eruptions the occurrence of superficially necrotic or haemorrhagic skin manifestations and the presence of an urticarial component could be of diagnostic value. Now that more experience in this particular field has accumulated, we propose to discuss in this paper once more our views on these syndromes with special reference to two recent cases.

CASE REPORTS.

CASE 1.—A woman aged 38.

Onset of eruption 2 years ago on legs and arms. The occurrence of the skin lesions was marked by remissions and exacerbations. When the patient took complete rest her condition improved, but became worse after physical effort.

When 6 years old the patient was treated for tuberculosis for six months.

Her husband and children are in good health. A child of her brother suffers from "eczema."

The use of drugs is denied.

On examination.—The skin eruption was found chiefly on the extremities with some lesions on the shoulders and on the face; it was most marked on the lower legs (Fig. 1). There irregular, poorly defined, erythematous macular lesions predominated, often with a somewhat livid colour in the centre and frequently merged into larger patches. Older parts showed a brownish-yellow hue. Sometimes the surfaces of these areas were made uneven by papular elevations. Among the erythematous patches small clear vesicles were observed. In some places over the macular lesions the epidermis was macerated, forming erosions surrounded by a collar of macerated epithelium. Numerous brownish-red crusts and scabs were seen.

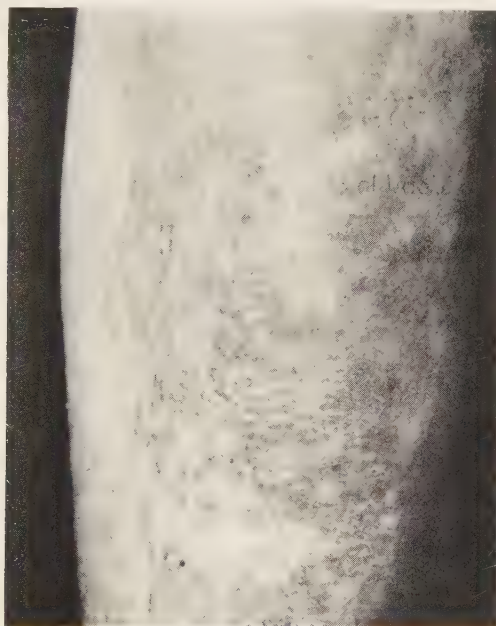


FIG. 1.

A conspicuous feature was the presence of firm, flat, pink to brownish-yellow, mostly circular papules, the size of a lentil to a pea. These mostly occurred singly, sometimes in groups, on the normal as well as on the affected skin. They were somewhat reminiscent of urticaria but were too firm and, lasting for several days, not transient enough. Some of them showed at the top a pinpoint-size vesicle or a small haemorrhagic scab. These papular elements were most marked on the knees and elbows, and some were present over the shoulder-blades.

Purpura was not clearly present. Only on the second examination, some weeks later, were a few slight, scattered, cutaneous haemorrhages found on the lower legs for the first time.

General physical examination elicited no pathological findings. Laboratory studies showed a normal blood picture. Blood pressure 140/85. E.S.R. 3 mm. after 1 hour. Urine: normal. Serological reactions against streptococci: normal. Otorhinolaryngological examination: normal. Edentulous. Skiagrams showed a few retained roots. From these granulomas *Streptococcus viridans* was cultured.

Histology (papular lesions).—In the corium nearly all the smaller blood vessels were severely affected, with swelling of the endothelium and inflammation and fibrinoid necrosis of the wall. The enlarged vascular wall was infiltrated by numerous inflammatory cells, mainly polynuclear leucocytes and some eosinophils. A considerable number of the leucocytes showed nuclear disintegration (leucoclasia). In addition fibroblasts, histiocytes and mononuclear cells were found. A few blood-vessels appeared to be normal. On serial section, however, it was apparent that in the same vessel normal parts occurred adjacent to seriously affected parts. At one place subepidermal vesicle formation was seen, containing fibrin, erythrocytes and leucocytes, among which eosinophils were present. In all sections the medium-sized arteries at the border between cutis and subcutis were unaffected. Micro-organisms could not be demonstrated in the sections.

Course.—Removal of the dental granulomas had no noticeable effect. Following treatment with terramycin there was a slight improvement. The patient eventually left hospital in the same condition as before, and was later readmitted. The skin changes could then be suppressed by cortisone, though there was a tendency to recurrence when the dose (100 mg. daily) was reduced.

This case bears considerable resemblance to one previously discussed in this journal (Ruiter, 1953). Both patients showed a symmetrical eruption predominantly on the extremities consisting of multiform macular lesions and firm, flat papules with an urticaria-like component. In the present case the brownish-red crusts and scabs remaining after the lesions subsided indicated a tendency towards extravasation of blood; they may be explained by the histological finding of slit-like vesicles containing scattered erythrocytes, leucocytes and fibrin. This tendency towards cutaneous haemorrhages, however, was much less pronounced than in our previous case in which purpura was a rather conspicuous feature of the eruption. On the other hand, in the case reported here, an exudative component, causing local maceration of the skin and giving rise to numerous minute and larger vesicles, came more to the fore than in our previous observation. Apart from these details, however, both cases were basically identical. They also showed similar histological changes.

The histological picture found in the patient presented here was that of a hyperergic vasculitis of the cutaneous vessels, the small dermal vessels being predominantly affected. Such a histopathological substrate in our experience corresponds with skin pictures ranging from so-called anaphylactic purpura to marked polymorphous eruptions. Elsewhere (Ruiter, 1952, 1948) are described vascular changes of the same nature corresponding, however, with skin eruptions seemingly differing in several respects. In these cases also the walls of the small dermal vessels showed fibrinoid changes, but the vascular and perivascular infiltrations were of a more subacute character, and the most severely affected vessels were those situated somewhat lower in the corium, in the region of the sweat glands. Apart from these details, however, the vascular changes revealed morphogenetically a close relationship with those observed in the former cases. Moreover, on analysing the skin picture,

both groups, in spite of the different aspect of the lesions, appeared to have a number of clinical features in common. They also seemed to be pathogenetically closely related; we therefore proposed to group these various cases together under the heading of allergic cutaneous arteriolitis.

The term allergic cutaneous arteriolitis indicates that we hold the view that an allergic pathogenesis in these syndromes is the most likely one. In this particular type of allergy, foreign proteins, drugs, and especially bacteria, are possible antigens. Now it is a well-known fact that the tissue response to these allergens may also result in granulomatous foci. Therefore, in accepting an allergic pathogenesis for allergic cutaneous arteriolitis, one might expect vascular inflammation of a markedly granulomatous nature. It is noteworthy that such changes can be found in a systemic disorder, recently described, of definitely allergic origin, in which beside lesions of the skin marked vascular changes in the internal organs are a conspicuous feature. This syndrome, which in our opinion represents in several respects an argument in favour of the allergic pathogenesis of so-called allergic cutaneous arteriolitis, can be demonstrated by the following case. This observation also seems to indicate that a relationship exists between allergic cutaneous arteriolitis and vascular changes of the same character affecting the internal organs.

CASE 2.—A woman 55 years of age. Since March 1951 she complains of fatigue and coughing. The coughing occurs in attacks, with small quantities of white sputum. More recently, wheezing and dyspnoea developed. During the last 10 years she has been very susceptible to respiratory tract disorders. In June 1951 nodules appeared on the legs, remaining for a month or so.

No history of drugs, and contact with beryllium can be excluded.

Family history.—Father, a niece and several uncles and aunts suffer from asthma.

Skin (17. vii. 1951).—An eruption of erythematous spots and reddish flat cutaneous-subcutaneous nodules, some showing slight scaling, was observed on the lower legs (upper third part) and in the region of both knees (Fig. 2). In some places these elements showed a tendency to coalescence and here and there an indication of a net-like arrangement was found. There was no itching or pain.

When seen later (22. viii. 1951) the skin lesions had subsided, leaving some pigment. On 19 May 1952 a few coin-size erythematous macules with a tendency towards central regression were seen on the backs of both hands. Ten days later these had mostly decreased in size.

General examination (August 1952) summarized.—Skiagram of the lungs: hilar glands slightly enlarged; numerous small miliary infiltrates especially in the middle and lower fields. Heart: normal.

Liver and spleen not palpable.

Blood picture: Hb 98%. R.B.C. 5,980,000. W.B.C. 4600. Eos. 1%.

B.P. 140/90. E.S.R. 53 mm./1 hr.

Urine: no albumen or glucose; some leucocytes and bacteria (enterococci and coliforms).

Serum bilirubin direct negative; cholesterol 231 mg.%, cholesterol esters 147 mg.%, calc. formolgel test 5 tubes positive; alkaline phosphatase 16 units; thymol turbidity 5.9 units. Pirquet reaction: negative.

Antistreptolysin titre 130 units.

Temperature 37.5°.

The teeth were in bad condition.

Otorhinolaryngological examination: sinuses translucent. The pale bluish hue of the nasal mucosa suggested an allergic condition.

Histological examination of supraclavicular lymph gland: slight non-specific inflammatory changes.

Liver biopsy: In the liver tissue were very small granulomas not typical of tuberculosis or sarcoid.

Histology.—At low magnification numerous inflammatory foci were seen in the corium and in the fatty tissue, often having a small vessel in the centre. In some

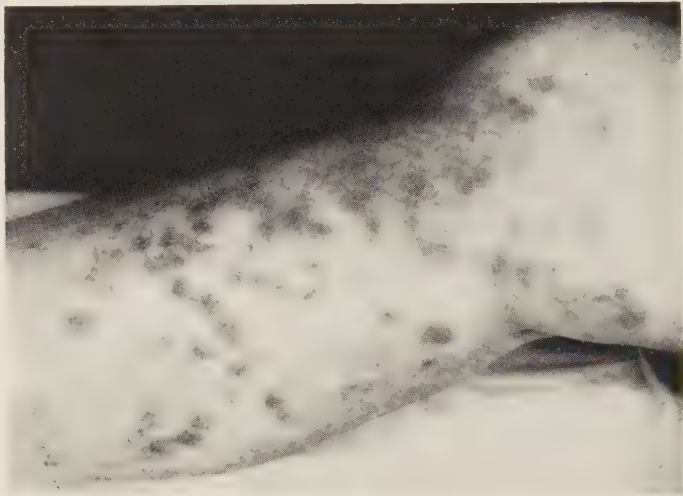


FIG. 2.

sections an affected dermal arteriole cut lengthwise and surrounded by a granulomatous cuff could be followed for a fairly long distance (Fig. 3).

At higher magnification the endothelial cells of the small subpapillary vessels were swollen with perivascular oedema and infiltration. Deeper in the corium these areas were larger and more severe. The walls of the small blood vessels there showed fibrinoid necrosis, often restricted to a segment of the wall. The affected vessels were surrounded by a mantle of inflammatory tissue, consisting of a dense accumulation of fibroblasts and histiocytes, some resembling epithelioid cells; there were also lymphocyte-like cells while in some places multinucleated giant cells were found, mostly of the foreign-body type, less often of the Langhans type. Partly disintegrated polymorphonuclear leucocytes were occasionally met with, and here and there an eosinophil leucocyte. Sometimes the affected blood vessels could hardly be traced back; then, in the centre of the granuloma, a small area of fibrinoid necrosis was found, suggesting the remains of a vessel wall.

Distinct formation of granulomas was found at the border between cutis and subcutis. There some granulomas were clearly perivascular (Fig. 4), but in others the relationship to the vascular changes was less obvious. The medium-sized arteries of the subcutis, as far as they could be followed up in serial sections, were normal.

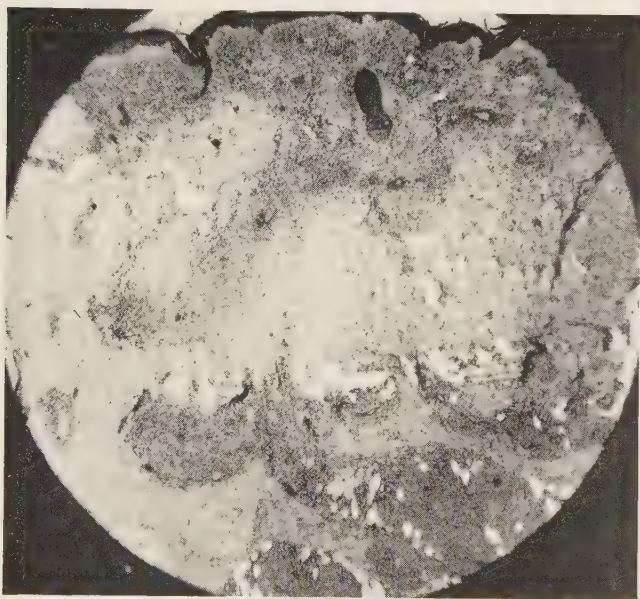


FIG. 3.

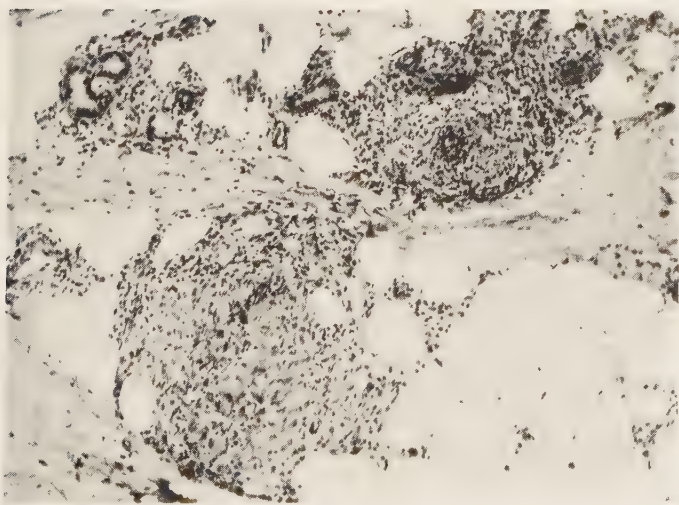


FIG. 4.—(case 2). At the left bottom sarcoid-like granuloma. At the right top perivascular granuloma ; the vascular wall showing fibrinoid necrosis.

Course.—ACTH was given and in the course of this treatment considerable improvement of the lung picture was observed. After she left hospital, however, the condition relapsed with a distinct increase of the spotty infiltration of the lungs. She was then nursed at home and did not return to the clinic until one year later. It was then found that the condition had improved gradually: the skin eruption had not recurred. The E.S.R. was still 31 mm./hr. The total serum protein was 8.16%, albumin 4.70%, globulin 3.37%. A more detailed examination was not possible at this time.

The histological picture of the skin in this case was mainly characterized by the presence of granulomas in connection with small cutaneous vessels (in the first place arterioles). The walls of the vessels involved showed fibrinoid necrosis, often segmental. Although some granulomas, especially in the subcutis, gave the impression of being situated extravascularly, in several of them a small vessel or the remnant of a vascular wall could be demonstrated by means of serial sections. In others the relationship to vascular changes was less clear, but the possibility exists that the affected vessels may have been incorporated completely in the granulomatous foci. It is noteworthy that the histological picture of the skin was somewhat reminiscent of that found in sarcoidosis.

The condition described here is in our opinion very closely related to, if not identical with, a syndrome described by Strauss *et al.* (1951a, b) as allergic granulomatosis. This syndrome was characterized by "severe allergy, fever and eosinophilia, accompanied by systemic manifestations (vascular, cardiac, pulmonary, gastro-intestinal, renal and cutaneous)". The skin lesions consisted of: (i) erythematous maculo-papular eruptions resembling erythema multiforme; (ii) haemorrhagic lesions, sometimes accompanied by necrosis and often associated with urticarial elements (similar to Schoenlein's purpura); and (iii) subcutaneous and cutaneous nodules. They occurred singly or in numbers or followed one upon the other during the course of the disease and tended to occur in crops. The cutaneous manifestations were accompanied by changes in various internal organs in which vascular involvement played a major part. In addition to processes resembling periarteritis nodosa granulomatous lesions of the vessels were found, with perivascular granulomas frequently showing fibrinoid necrosis. These lesions were widely disseminated in blood vessels and connective tissue throughout the body. The histopathological changes of the skin appeared to be essentially identical with those found in the internal organs, comprising exudative inflammatory lesions of the small cutaneous vessels with fibrinoid necrosis, leucoclasia and eosinophilia.

Between the cases of Strauss *et al.* and the condition described in our second patient some differences appear to exist. In the former the relationships between the granulomas and the vascular changes were not always as distinct as in our patient, in whom also the acute exudative inflammatory lesions of

the capillaries and small vessels in the upper layers of the corium were less conspicuous. We think it possible that this may be explained by the fact that in most of Strauss's patients the disorder rapidly increased in severity. The pathological findings therefore mostly relate to autopsy reports. The course in our patient was a chronic one and the disease showed—as subsequently appeared—a tendency towards recovery.

Of the visceral lesions observed in our patient the most conspicuous ones were the changes in the lungs revealed by x-ray examination. We presume that these lesions, resembling sarcoid, must be granulomas identical with those observed in the skin; the granulomas found in the liver biopsy are in support of this view.

Strauss and his co-workers state that in their cases an allergic aetiology seems to be clearly proved, at least as long as asthma is considered to be an allergic manifestation. In this respect the frequent occurrence of asthma in the family history of our patient is worth noting. By many authors (e.g., Harkavy, 1943) a bacterial origin is suggested while other allergens may play an additional eliciting part.

Meanwhile allergic granulomatosis is probably not a new conception. In the literature various reports of cases are to be found, either identical with or showing great similarity to the syndrome described by Strauss and his co-workers. Teilum (1946) described an autopsy case in which disseminated focal processes, consisting of central necrosis most frequently around a small vessel with peripheral accumulation of epithelioid cells and giant cells, were observed in the internal organs. He referred in his article to a number of autopsy reports of other authors. Teilum accepted an allergic pathogenesis for his case and thought that for these syndromes the term arteriolitis granulomatosa allergica might be used. A relation between these cases and allergic granulomatosis seems highly probable.

We have included this syndrome in our discussion of allergic cutaneous arteriolitis because it seems to furnish some further arguments in favour of an allergic pathogenesis for the latter. Both syndromes, though pathogenetically closely related, differ in several other respects, and there are important clinical differences. Allergic cutaneous arteriolitis, its lesions usually being restricted to the skin, runs a more benign course, whereas allergic granulomatosis appears to affect many organs and to carry a doubtful prognosis.

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A LETTER FROM DENMARK.

POUL V. MARCUSSEN.

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SIR,—Small nations are handicapped in many respects but, on the other hand, also have certain advantages. The extent of this country (16,500 square miles), where the highest point is 564 feet above sea-level, makes it fairly easy for the 56 specialists of dermatology to meet more than once a year. Discussions on epidemiological variations within groups of diseases, for instance, which do not appear in published statistics, or on the siting of dermatological centres are rarely available in the literature. They may be of some interest as a basis for comparison and I have therefore chosen to deal with such discussions, instead of reporting scientific literature, with which your readers are no doubt familiar.

Mycotic infections are a steadily increasing problem with us, apart from the common ringworm acquired from cattle, which in spite of the agricultural progress of this country has remained at a constant level. Especially the incidence of mycotic infections of the feet is rapidly increasing. Up to the year 1913 only one case of interdigital epidermophytosis was diagnosed. In 1922 a total of 23 sporadic cases were traced. During the early thirties minor epidemics were observed in schools and colleges, and from this time onwards the numbers of cases treated in hospital have followed a rising linear curve, interrupted only by a slight fall during and after World War II (1941–7). This depression of the curve cannot be explained by the restrictions on hot water and soap, nor by the enforced interruption of communications with the western world, because a similar fall has been seen in the incidence of non-infectious diseases, e.g., psoriasis. In 1952, 2 cases per 1000 inhabitants were treated in hospital. The dermatophyte demonstrated was in practically all cases the fungus described by Kauffmann-Wolf and Priestley. Investigations carried out in 1948 showed, however, that 20% of the population over 10 years of age had asymptomatic infections, and that 20% of these developed symptoms within an observation period of ten months. We may thus calculate that within one year not less than 40 out of 1000 inhabitants have infections of the feet causing symptoms, and we judge that only one-tenth of these are submitted to dermatological treatment. It is a common impression that severe cases of generalized epidermophytid are rarer than previously.

Various comparative analyses of antimycotic drugs (unpublished) tend to show that treatment has made no definite progress. Careful hospital treatment

results in removal of the fungi in 80% of patients, but even this result requires so much enthusiasm on the part of patient and physician alike that the treatment has no chance of being generally adopted. On the contrary, patients with such lesions are inclined to treat themselves with drugs acquired at a dispensing chemist's and to discontinue the treatment as soon as the worst troubles have subsided. In 20% of patients with asymptomatic infection the fungi will disappear within ten months without treatment. It is worth noting that the Danish State Board of Health in 1937 was aware of the beginning epidemic and ordered all wooden bath-mats and duck boards to be removed from public bathing establishments and schools; but this did not alter the linear rise of the epidemic curve. There is much evidence to suggest that the disease, saprophytically, or as a subclinical or mild infection, tends to be pandemic, and that the severe clinical eruptions arise only in special circumstances. It has been shown that the rare infections of the interdigital parts of the hands occur exclusively in persons whose occupations expose them particularly to moisture, or in association with deformities of the fingers, or in those having special jobs, e.g., salesmen who carry heavy bags. The obvious significance of environment explains the excellent effect of simple drying up and of drugs with a mild or doubtful fungistatic action.

As early as in 1941 it was a generally recognized fact that 10% of the patients treated for mycotic infections of the feet were misdiagnosed cases of contact dermatitis caused by accelerators or anti-oxidants in rubber used in the manufacture of footwear. In this country rubber is responsible in 2-3% of all the cases of contact dermatitis in which there is a positive patch test. Speaking of contact dermatitis, it is a notable fact that 2% of our cases are caused by a certain sulpha-drug ointment which has maintained its popularity through more than 10 years despite all warning. Local treatment with antibiotics, on the other hand, is not used to any great extent. This fact facilitates the use of routine patch-test series, which have grown increasingly important, not the least so in the diagnosis of dermatitis due to over-treatment. Tars and mercury follow next to varieties of primula as the most common sensitizers.

Ringworm of the scalp has in the last 50 years been regarded as a rare phenomenon; the last school epidemic was described in 1907. During the past 6 or 7 years sporadic cases of infection with *Microsporon canis* have occurred with increasing frequency, and we have the impression that this is the precursor of an epidemic. *Microsporon audouini* has been demonstrated in few cases only. Favus was recently discovered in two Danish children; the infection seems to have been reintroduced during the war by refugees.

While the man-in-the-street seems rather uninterested in fungous diseases, warts, in particular plantar warts, are regarded as a lesion that must be cured at almost any cost. The first case of plantar warts was demonstrated in 1901 at a meeting of the Danish Dermatological Society. The correctness of the

diagnosis was extensively discussed. Up to 1925 only a few such cases were submitted to treatment. The introduction of irradiation therapy, which in practice centralized the treatment of this lesion, has made it possible to observe its variations in Copenhagen with some accuracy. Since 1935 the incidence of plantar warts has risen rapidly without responding to hygienic measures, and even uninfluenced by World War II. In 1952 the incidence was 8 per 1000.

From an epidemiological point of view it is worth noting that in this country plantar warts are just as frequent as reported cases of whooping cough, and mycotic infections as frequent as acute tonsillitis. Seen from this aspect dermatology is not devoid of problems and work.

The bacterial infections, on the other hand, are declining. The incidence of lupus vulgaris, for which we have fairly certain data since the year 1900, was 0.5 per 10,000 inhabitants per annum during the period 1900-5. Within the past 10 years the incidence has remained fairly constant at 0.05 per 10,000.

The much discussed fact that lupus vulgaris formerly was unknown in Greenland, where there is no stock-keeping, but where the incidence of human tuberculosis is high, was no doubt due to the population numbering less than 20,000, being thus too small to warrant a case of lupus vulgaris. The first case was demonstrated in 1947.

The total cases of lupus vulgaris in Denmark have decreased from 10 to 1 per 10,000 inhabitants. A certain accumulation of non-cured cases was due to the cure rate of the Finsen treatment being 70%. Forty per cent. of these accumulated cases appear cured since the introduction of calciferol treatment, and the rest seem to respond to isonicotinic acid hydrazide, alone or in combination with para-aminosalicylic acid. Among the recently discovered cases of lupus vulgaris approximately half are of fairly long standing. In the fresh cases, especially in young subjects and those with a weakly positive tuberculin test, calciferol treatment has proved very dangerous as it brings about a spread of the tuberculous process. The policy of BCG vaccination, now extended to all negative reactors, has caused less than ten mild and easily cured cases of lupus vulgaris, but a few serious cutaneous and surgical complications. It may be stated, for the sake of comparison, that the incidence of syphilis in Copenhagen is 0.1 per 1000 against 3 per 1000 in 1945.

The above-mentioned variations in morbidity might be expected to have brought about a fundamental change in the dermatovenereological specialty. However, other variations in morbidity and opportunities for treatment seem to have compensated for these.

Dermatological departments in this country still comprise 1.4 beds per 10,000 inhabitants, distributed over one state, three municipal, and three private hospitals, situated in five cities. This number of beds is hardly sufficient for the treatment of all acute and extensive cases. A remarkable

fact is the rising interest in dermatology, especially among general practitioners, specialists of internal medicine, and within the Danish State Board of Health. A questionnaire recently disclosed that general practitioners desire increased facilities for studying dermatology (and paediatrics). At the suggestion of the Director of the Danish State Board of Health (who judiciously has maintained his sole function of adviser) each county throughout the country builds up a central hospital comprising various special departments. This has resulted in a migration of young, exceedingly well-trained dermatologists to smaller towns with the object of becoming consultants or department leaders at these new hospitals. As a consequence of this development a specialist of dermatology is already now available within a distance of 30 miles of any part of the country, and it helps to relieve local radiological, internal-medical, and non-specialist departments of the burden of dermatological patients.

I am,

Yours faithfully,

POUL V. MARCUSSEN.

BOOK REVIEWS.

THE CUTANEOUS MANIFESTATIONS OF SYSTEMIC DISEASES.*

This is a very slim volume consisting of thirteen lectures given to medical students and is accompanied by some fifty black and white illustrations of fair quality. Dr. Downing discusses a large number of eruptions developing in systemic illnesses but in such a brief manner and with paragraphs so disjointed that the text does not make smooth reading.

The book is well printed with an attractive soft black cover but its price of thirty-one shillings puts it into the luxury class. S. C. G.

AIDS TO DERMATOLOGY.†

DR. MACKENNA, aided for the first time by Dr. Lipman Cohen, continues his task of preparing an essence of dermatology for the use of beginners. The process of distillation might readily yield a product unpalatably strong and lacking in individual flavour. In fact it is agreeably smooth and will upset only the fastidious.

A minor criticism is that general therapeutics are discussed immediately after anatomy and physiology and before the student has been instructed in the terminology and morphology of skin lesions.

The drawing of the normal histology of the skin appears to have been omitted by error. The order of chapters seems a little arbitrary. Although diseases caused by animal parasites, fungi, tubercle bacilli, etc., are described in sequence, virus diseases appear six chapters later. Urticaria, eczema and purpura might logically appear in closer company and a mention of lichen simplex could reasonably appear in the chapter devoted to "The Lichens." The main emphasis is rightly on common diseases. Moniliasis, however, is very briefly discussed while the rare deep mycoses occupy several pages. Hebra's prurigo is a disease unfamiliar to the rising generation of dermatologists, yet it is described before Besnier's. An unusually sharp distinction is made between infantile atopic eczema and "sensitization" eczema due to alimentary allergens.

The student would gladly be spared unnecessary names. It is sufficient that he know the blisters of zoster are often bloody without noting the special title of "herpes zoster haemorrhagicus."

In general, the text is well up to date, and, used in conjunction with an atlas, it should be of use to students intimidated by more voluminous texts.

P. J. H.

* *The Cutaneous Manifestations of Systemic Diseases.* By JOHN GODWIN DOWNING. 1954. Charles C. Thomas, Illinois, U.S.A. Oxford: Blackwell Scientific Publications. Pp. 146. 52 Illustrations. Price 31s.

† *Aids to Dermatology* (4th ed.). R. M. B. MACKENNA and E. LIPMAN COHEN. London: Baillière, Tindall and Cox, 1954. Pp. 296. Price 7s. 6d.

OBITUARY.

DR. ROBERT AITKEN.

MEMBERS of the British Association of Dermatology will regret to hear of the death of Robert Aitken on 17 March, and many will recall his successful presidency of the Annual Meeting at Edinburgh in 1950. He had been a member of the British Association of Dermatology since 1922.

Dr. Aitken was born in Edinburgh in 1888 and graduated M.B., Ch.B., from Edinburgh University in 1911. After a period in general practice with the late Dr. Crerar in Maryport he commenced the study of dermatology under Sir Norman Walker who encouraged what proved to be a lifelong interest in lupus vulgaris: this was the subject for his thesis for M.D. During the Great War he served as a surgeon in the Royal Navy with the Grand Fleet and in the Mediterranean. In 1917 he became M.R.C.P.Ed., and was elected F.R.C.P.Ed. in 1921.

After his war service he resumed his dermatological work and was appointed to the staff of the Edinburgh Royal Infirmary. He was promoted to full physician in 1933 and made a lecturer in dermatology to Edinburgh University. He was particularly interested in cutaneous tuberculosis and ultra-violet light and organized a Finsen-Lomholt light department which did much useful work. His publications included two books, *Ultra-violet Radiations and Their Uses* and *The Problem of Lupus Vulgaris*, as well as papers on various other and related subjects. His hobbies included music, photography and yachting, and those who attended the Annual Meeting of the Association in 1937 and enjoyed the trip on the Firth of Clyde in his cabin-cruiser will not forget a delightful experience.

Heart disease prevented him from enjoying many other aspects of open-air life. Since his retirement from the Royal Infirmary in July 1953 he had suffered constantly from ill health, so that his end when it came was a merciful relief. It was sad that he was not permitted to enjoy his retirement as he would have liked. His colleagues will join in expressing sympathy with his family in their loss.

G. A. G. P.

CURRENT LITERATURE.

THE ROLE OF EMOTIONS IN DERMATOSES. G. M. FRUMESS. (1953) *J. Amer. med. Ass.* 152, 1417.

A very readable general review without original observations. Some of the author's generalizations are rather too sweeping and even the most ardent advocate of the importance of the role of the psyche in the production of skin disease will be provoked to an occasional protest.

A. J. R.

GRANULOMA FOLLOWING SWIMMING POOL ABRASIONS. B. REES and J. H. BENNETT. (1953) *J. Amer. med. Ass.* 152, 1606.

Nine cases of clinical tuberculosis verrucosa cutis following abrasions sustained in swimming pools are reported. Eight of the patients had been in the same pool. Tubercle bacilli were not found although serial sections were examined. Silica granuloma was excluded with the polariscope. The fact that two of the cases responded to isonicotinic acid hydrazide is not necessarily proof of a tuberculous origin.

A. J. R.

CHLOROQUINE DIPHOSPHATE IN TREATMENT OF DISCOID LUPUS ERYTHEMATOSUS.

L. GOLDMAN, P. COLE and H. PRESTON. (1953) *J. Amer. med. Ass.* 152, 1428.

A brief preliminary account of the clinical trial of chloroquine diphosphate in chronic discoid lupus erythematosus. The results appear to be comparable with those obtained with mepacrine, and chloroquine is less toxic.

A. J. R.

NEW APPROACH TO THE TREATMENT OF INTRACTABLE VERRUCA PLANTARIS (PLANTAR WART). H. L. DU VRIES. (1953) *J. Amer. med. Ass.*, **152**, 1202.

Plantar warts beneath the metatarsal heads can be disabling and intractable. Twenty-one cases were treated by excision of the condylar processes of the metatarsal heads. Good results are claimed.

A. J. R.

DERMATOSES AMONG OFFICE WORKERS. G. E. MORRIS. (1953) *J. Amer. med. Ass.*, **152**, 1218.

Thirty-six of 1213 patients with proved industrial dermatitis were office workers. The following causes were established: carbon paper 4; paper 5; glue 6; machine dyes and inks and the chemicals used to remove them 12; cardboard 2; rubber finger tops 3; rubber bands 1; paper towels 1; green paint on pencil 1; liquid soap 1. Three of the more unusual case histories are reported.

A. J. R.

INCREASED MITOTIC ACTIVITY AND NECROSIS FROM SENSITIZING AGENTS. EUG. BUJARD, W. JADASSOHN, R. BRUN and R. PAILLARD. (1953) *Acta allergol.*, **6**, 161.

Four cutaneous sensitizers of the dinitrochlorobenzene group were applied to the nipple of an unsensitized guinea-pig. A 1/1000 dilution caused increased mitosis and a 1% dilution produced necrosis. This effect was not produced by non-sensitizing substances of the same group.

H. T. H. W.

INVESTIGATIONS ON THE SERUM OF A CASE OF ATOPIC ECZEMA. F. UKRAINCZYK-LABORIE and R. LABORIE. (1953) *Acta allergol.*, **6**, 226.

Elimination of flour and milk from the diet of an adult atopic patient caused remission of symptoms on two occasions. Relapses followed a return to full diet. Investigations showed hypoglycaemia, hypercholesterolaemia and a low serum lipase. Pancreatic disturbance appeared to be part of the allergic diathesis.

H. T. H. W.

THE EFFECT OF ACTH AND CORTISONE TREATMENT IN SOME SKIN DISEASES. S. HELLERSTROM, E. HOLSTROM, S. HARD and B. MAGNUSSON. (1953) *Acta derm. venerol., Stockh.*, **33**, 285.

ACTH and cortisone have a salutary effect on cutaneous lesions and general symptoms of acute lupus erythematosus. Some improvement occurs in psoriasis and temporary improvement in exfoliative dermatitis, prolonged treatment keeping such patients relatively clear. Rapid and transient effect occurs in atopic eczema. Complications are Cushing's syndrome or tendency to infections, minor electrolyte balance disturbance and slight rise in blood pressure. In 2 cases of pustular psoriasis and acute lupus erythematosus spread of lesions occurred.

G. A. H.

CUTANEOUS ABSORPTION STUDIES USING RADIOPHOSPHORUS. M. HELDE and G. SEEBERG. (1953) *Acta derm. venerol., Stockh.*, **33**, 290.

Cutaneous absorption studies using radiophosphorus in different skin areas.

G. A. H.

SARCOIDOSIS INVOLVING THE HEART. I. GILG. (1953) *Acta derm. venerol., Stockh.*, **33**, 318.

A survey of the literature of sarcoidosis involving the heart. A case is described, a 45-year-old man with pulmonary sarcoidosis.

G. A. H.

FAMILIAL BENIGN CHRONIC PEMPHIGUS (HAILEY AND HAILEY) TREATED WITH CORTISONE. R. A. WEHNERT. (1953) *Acta derm. venerol., Stockh.*, **33**, 211.

Cortisone was effective in 3 cases of Hailey-Hailey disease so treated; 7 cases in all are clinically described.

G. A. H.

CYANCOBALAMIN (VITAMIN B₁₂) THERAPY OF LUPUS ERYTHEMATOSUS: FURTHER OBSERVATIONS. S. GOLDBLATT. (1953) *Acta derm. venerol., Stockh.*, **33**, 216.

Seventeen cases of lupus erythematosus (2 acute disseminated, 5 subacute disseminated, 10 chronic discoid) were treated with intramuscular injections of vitamin B₁₂ in doses of 15 to 1000 micrograms.

No toxic effects followed the large doses for long periods and in adequate dosage systemic symptoms were relieved and skin lesions underwent involution.

Fifteen mg. at weekly intervals are recommended for chronic discoid cases (though "100 mg. daily would speed recovery") and daily treatment with 100-1000 mg. for 1-2 weeks for disseminated cases. Maintenance doses in all cases should be given for months after initial healing.

G. A. H.

PSEUDO-EPITHELIOMATOUS HYPERPLASIA. J. SOMMERVILLE. (1953) *Acta dermat. venereol., Stockh.*, **33**, 236.

A comprehensive account of the history and literature and a discussion of various criteria for differential histological diagnosis which should be read in full.

G. A. H.

ACTH THERAPY IN LICHEN RUBER PLANUS. A. KRISTJANSEN and F. REYMANN. (1953) *Acta dermat. venereol. Stockh.*, **33**, 205.

Six patients with long continued lichen planus resisting ordinary measures responded to ACTH for two weeks. Four were symptom free 16, 11, 9 and 8 months later. On 2 there was no effect. No change took place in mucosal lesions. Two acute cases showed total resolution of lesions but the follow up period was too short for definite conclusions to be made. ACTH should be reserved for chronic non-responsive cases of lichen planus.

G. A. H.

MIDDLEBROOK'S REACTION IN BOECK'S SARCOID, LUPUS VULGARIS AND ERYTHEMATODES. K. ODEGAARD. (1953) *Acta dermat. venereol., Stockh.*, **33**, 181.

Middlebrook's test with old tuberculin as antigen on 86 sera of patients with diseases not related to tuberculosis gave a positive reaction in 10, negative in 76. In 19 pulmonary tuberculosis patients 13 positive, 6 negative; in 20 lupus vulgaris 13 positive, 7 negative; in 18 lupus erythematosus 10 positive, 8 negative; in 19 Boeck's sarcoid 5 positive, 14 negative.

G. A. H.

ON THE OCCURRENCE OF ERYTHEMA NODOSUM IN ASSOCIATION WITH GONORRHOEA. C. E. SONCK. (1953) *Acta dermat. venereol., Stockh.*, **33**, 188.

From a study of 4188 cases the author concludes that gonorrhoea is not one of the types of infection associated with erythema nodosum.

G. A. H.

CAPILLARY MICROSCOPY IN THE DIFFERENTIAL DIAGNOSIS OF SKIN DISEASES. O. GILJE. (1953) *Acta dermat. venereol., Stockh.*, **33**, 303.

Capillary microscopy concerns the study of superficial cutaneous vessels under direct illumination after the skin has been made transparent by oil applied to it. The normal capillary microscopic appearance is described and compared with the pictures seen in the common skin diseases. Photographs illustrate the thesis.

G. A. H.

A LABORATORY INFECTION CAUSED BY HISTOPLASMA CAPSULATUM. A. NILZEN and H. PALDROK. (1953) *Acta dermat. venereol., Stockh.*, **33**, 329.

Seven patients developed symptoms suggesting bronchopneumonia after working in a laboratory where experimental work with *inter alia* Histoplasma capsulatum was in progress; the histoplasmin test was positive and the coccidioidin test negative in all cases.

G. A. H.

LYMPHADENOSIS BENIGNA CUTIS AS A SYMPTOM OF MALIGNANT TUMOURS. B. BÄFVERSTEDT. (1953) *Acta dermat. venereol., Stockh.*, **33**, 171.

Lymphadenosis benigna cutis may be a manifestation of a peculiar reaction of tissue, local or widespread, to stimuli of different kinds. In the immediate neighbourhood of tumours there are often inflammatory reactions having lymphadenoid structure. This syndrome produced by or associated with malignant tumours may not necessarily be localized to the skin. Three cases of malignant tumours (dermatosarcoma protuberans, squamous celled epithelioma of the skin and cancer of the oesophagus) probably gave rise to dispersed lymphadenosis benigna cutis.

G. A. H.

SENSITIZATION TO COBALT IN POTTERY WORKERS. V. PIRILA. (1953) *Acta dermat. venereol., Stockh.*, **33**, 193.

Patch tests were made on 641 workers to determine the frequency of sensitization to cobalt in a Finnish pottery works. A strong reaction to 5% cobalt nitrate was obtained in 9 cases of previous or present dermatitis. (Cobalt is added to different clays to neutralize the faint yellow

colour of iron oxide). The dermatitis settled in 3 cases where it was possible to avoid cobalt in the clays handled. G. A. H.

A CASE OF REITER'S SYNDROME TREATED WITH CHLORAMPHENICOL. DAVID WHEATLEY. (1953) *Brit. J. vener. Dis.*, 29, 162.

A male aged 38 with the triad of cystitis, conjunctivitis and arthritis was treated with chloramphenicol and the symptoms and pyuria rapidly resolved. No publication of such a case treated with chloramphenicol could be traced in the English literature, although one such report had appeared in America. W. G. A.

MASKED PERFORATION OF A GASTRIC ULCER IN A CASE OF TABES DORSALIS. J. OLIVER DOYLE and DOUGLAS J. CAMPBELL. (1953) *Brit. J. vener. Dis.*, 29, 164.

A case of masked perforation of a gastric ulcer in a tabetic is presented, suggesting that in tabes dorsalis visceral pain may be diminished or even absent. The difficulties in diagnosis are stressed and the relevant literature briefly discussed. W. G. A.

POTASSIUM IODIDE IN THE TREATMENT OF SYPHILIS. P. KEEN. (1953) *Brit. J. vener. Dis.*, 29, 168.

The role of potassium iodide in the treatment of syphilis is discussed. Four cases of bone syphilis treated with potassium iodide are described. It is suggested that the clinical and radiological evidence in these cases shows that potassium iodide can accelerate the resolution of certain syphilitic lesions and it is further suggested that a preliminary intensive course of potassium iodide, details of which are given, should be given to all patients showing dense sclerotic bone lesions. The author concludes by stating that, despite modern methods of treating syphilis, potassium iodide is still a useful adjunct in the treatment of bone syphilis, particularly in the Bantu of South Africa. W. G. A.

IMPETIGO HERPETIFORMIS IN A MALE. G. TRIMIGLIOZZI. (1953) *Dermatologia*, 4, 168.

This case (of which the widespread distribution can be seen from the photographs) was helped by aureomycin and not by small doses of cortisone or ACTH. Although this might point to an infective theory, the low value of the 17-ketosteroids suggests an endocrine basis for this peculiar eruption. D. S. W.

ERYTHEMA ANNULARE CENTRIFUGUM OF UNCOMMON SEVERITY. V. CIAULA. (1953) *Dermatologia*, 4, 107.

A review of the case and discussion on the differentiation from the other annular erythemas. There was a favourable reaction to intravenous antihistamines. The author suggests an allergic cause. D. S. W.

FLUORESCIN TEST IN EVALUATION OF VITALITY OF PLASTIC PEDICLES. A. R. COFANO and S. ROMANO. (1953) *Dermatologia*, 4, 147.

An explanation of the use of an intravenous solution of fluorescein with subsequent observation under Wood's light, to determine the vascular continuity of pedicles; 10 c.c. of a 10% solution was used. As other authors have done, they remark on its freedom from any side effects or toxicity. D. S. W.

MEPACRINE TREATMENT OF LUPUS ERYTHEMATOSUS. A. APRA. (1953) *Dermatologia*, 4, 206.

The author has treated 19 cases with doses ranging from 100 to 300 mg. a day for one to three months. He claims fifteen excellent results and only one case of intolerance. This occurred in a man on the twentieth day of treatment and consisted of vomiting, diarrhoea and malaise with some fall in the leucocyte count. I have recently had a case of agranulocytosis during mepacrine treatment, and this hazard, as well as the skin eruptions that may occur, should be borne in mind by those who use it. D. S. W.

ISONICOTINIC ACID HYDRAZIDE IN SKIN TUBERCULOSIS. A. MARCHIONINI and H. ROCKL. (1953) *Dermatologia*, 4, 161.

108 cases (of which the great majority were lupus) were treated with a dose of 10-15 mg. per kilo body weight. Side effects were surprisingly few in this dosage—which is higher than that

usually given in this country. Improvement was rapid and consistent in the cases of lupus and was said to be helpful in a case of papulo-necrotic tuberculide; three out of four cases of Bazin's disease were said to have healed. The authors remark that clinical cure does not necessarily correspond with histological cure. They discuss the histological picture under treatment.

Those patients who suffered gastro-intestinal upset were relieved either by taking milk at the same time or, if severe, by an intravenous use of the drug—a procedure well tolerated.

D. S. W.

SURFACE-WETTING AGENTS IN DERMATOLOGY. P. NAZZARO. (1953) *Dermatologia*, 4, 195.

An excellent and full account of the types and composition of the various surface-wetting agents, and a discussion on their mode of action, use and limitations. This should be read by anyone with an interest in the pharmaceutical aspect of dermatology and, indeed, by all who use these agents in topical application or in ointment bases.

D. S. W.

BULLOUS CONGENITAL ICHTHYOSIFORM ERYTHRODERMA. LESLIE P. BARKER and WILBERT SACHS. (1953) *Arch. Derm. Syph., Chicago*, 67, 443.

After a careful study of a case and a survey of the literature the authors conclude that ichthyosiform erythroderma, with or without bullae, ichthyosis and ichthyosis hystrix are variants of the same disease and that the microscopic change is primarily in the granular layer of the epidermis.

J. K.

MYCOSIS FUNGOIDES—FURTHER REPORT ON CASES OF SUCCESSFUL TREATMENT WITH ANTIMONIALS. JOHN GARB. (1953) *Arch. Derm. Syph., Chicago*, 67, 463.

From personal experience and reports by others the author reaffirms his belief in the efficacy of antimony in some cases of mycosis fungoides. In these cases its action is not merely palliative but curative. Tartar emetic is more effective than the milder antimonials.

J. K.

PHYSIOLOGIC STUDIES IN ATOPIC DERMATITIS (DISSEMINATED NEURODERMATITIS)—I. THE LOCAL CUTANEOUS RESPONSE TO INTRADERMALLY INJECTED ACETYLCHOLINE AND EPINEPHRINE. WALTER C. LOBITZ, JR., and CLARENCE C. CAMPBELL. (1953) *Arch. Derm. Syph., Chicago*, 67, 575.

While the response to epinephrine is normal, after intradermal injection of acetylcholine there is a marked delay in the development of the blanched area beyond the injection wheal in cases of atopic dermatitis. The authors conclude that these patients give a vasoconstrictor response to acetylcholine.

J. K.

RETICULOENDOTHELIAL CELL HYPERPLASIA IN RELATION TO ANTIMONIAL THERAPY OF MYCOSIS FUNGOIDES. JOHN GARB and CHARLES F. SIMS. (1953) *Arch. Derm. Syph., Chicago*, 68, 1.

This article sets out to try to show that the success of antimony therapy in mycosis fungoides is commensurate with hyperplasia of reticuloendothelial cells, but the conclusion is that there is no proof of a positive correlation. The article, however, is worth study for its careful compilation and its extensive references to the literature of the aetiology of this disease.

J. K.

CHANGES OF CLIMATE AND ENVIRONMENT IN TREATMENT OF DERMATOLOGIC DISEASES—EFFECT ON NEURODERMATITIS AND CERTAIN OTHER CHRONIC DERMATOSES. LESLIE M. SMITH and H. D. GARRETT. (1953) *Arch. Derm. Syph., Chicago*, 68, 28.

We are all aware of the benefit of a change of environment, especially to a dry sunny climate, in such cases but, though the authors show that such things do happen in Texas, they justly point out that change of emotional environment is just as important as change of physical environment, and the business man who insists on keeping in touch with New York by telephone is certainly not going to receive the same benefit as the man who can forget all his worries and relax.

J. K.

AETIOLOGY OF NUMMULAR ECZEMA. L. P. FOWLE and J. W. RICE. (1953) *Arch. Derm. Syph., Chicago*, 68, 69.

From a careful experiment the authors conclude that staphylococci are important in nummular eczema both by invasion of the skin and by producing bacterial allergy. Hypovitaminosis not

only of vitamin A but, often more important, of folic acid and the vitamin B complex may also be a factor. J. K.

COMPLEMENT IN DISSEMINATED (SYSTEMIC) LUPUS ERYTHEMATOSUS. JOSEPH A. ELLIOTT, Jr., and DON R. MATHIESON. (1953) *Arch. Derm. Syph., Chicago*, **68**, 119.

The authors have estimated the amount of complement in the blood of patients suffering from disseminated lupus erythematosus by finding the amount of serum required to haemolyse sheep's red cells. There was a correlation between activity of complement and albuminuria, serum albumin value, E.S.R., results of complement fixation tests for syphilis, leucocyte counts, presence of lupus erythematosus cells, skin lesions and fever. No correlation was noted with serum globulin value, results of flocculation tests for syphilis and arthralgias. J. K.

FLUORESCENCE OF MICROSPORUM AUDOUINI-INFECTED HAIR. I. CHEMICAL AND SPECTROSCOPIC STUDIES. HARRY M. ROBINSON, Jr., FRANK H. J. FIGGE and EUGENE S. BERESTON. (1953) *Arch. Derm. Syph., Chicago*, **68**, 129.

The fluorescent substance was extracted from infected hairs by boiling with distilled water. It is a white powder, insoluble in organic solvents, shows maximum fluorescence at pH 6.5 and is destroyed by strong acids and alkalis. The spectrograph showed a wide band with a maximum at 4902 Å, and it was concluded from infra-red absorption spectra that the substance has a small molecule, resembles a peptide and contains a —CONH—, an —OH, CH₃ and an =NH group. J. K.

ARTHROPODS OF DERMATOLOGICAL INTEREST. ORLANDO CANIZARES and HARRY SHATIN. (1953) *Arch. Derm. Syph., Chicago*, **68**, 157.

This is a useful and comprehensive list with notes which, though they refer mainly to the American continent, occasionally mention the rest of the world. J. K.

STUDIES OF PLASMA CHANGES IN SKIN DISEASES BY PAPER CHROMATOGRAPHY. F. KALZ, P. TELNER, J. H. QUASTEL and S. F. VAN STRATEN. (1953) *Arch. Derm. Syph., Chicago*, **68**, 167.

This reprint of a paper read at the Tenth International Congress of Dermatology in London in 1952 describes the methods used and concludes that though the method has no specific diagnostic value it permits assessment of the activity of a disease process in which protein changes are prone to occur. J. K.

ADVANCES IN THE TREATMENT OF SKIN DISEASES. GODFREY BAMBER. (1953) *Practitioner*, **171**, 378.

Isoniazid is being used in the treatment of lupus vulgaris with good results, streptomycin sometimes being given at the same time. ACTH and cortisone can, in some crises, tide over a patient, but it seems unlikely they will ever help the general practitioner in his daily round. Sensitization to penicillin and streptomycin is occurring not only in patients but in doctors and nurses who give the injections. In Liverpool, 10% of the district nurses have become sensitive to one or both drugs. The efficacy of several skin disinfectants was tested against *Staph. pyogenes*, *B. coli*, *Ps. pyogenes* and *Proteus vulgaris*. All the test organisms were killed within 30 seconds by 1% iodine or 1% cetrimide in 70% industrial spirit, but the same concentration of spirit without any additional substance was practically as good, while cetrimide in aqueous solution did not give such good results.

The part of the chemical structure of a compound to which a patient reacts may be present in what may appear to be totally dissimilar substances. The para-amino group is a common cause of sensitization and is found in paraphenylene hair dyes, para-aminosalicylic acid, the sulphonamides, and local anaesthetics such as procaine and benzocaine, so the real reason why a woman develops a rash after her hair has been dyed, when this has been done with impunity on previous occasions, may be because, in the interval, she has been given injections of procaine penicillin or has been using an ointment containing benzocaine for pruritus vulvae.

In senile pruritus, therapy with a combination of both androgen and oestrogen is sometimes helpful and avoids the unwanted results of hormonal imbalance such as may be produced by giving either substance by itself.

Papaverine hydrochloride, 1 g. intravenously, will usually relieve or abolish itching for several hours, and can be repeated without losing its efficacy. It has no narcotic action. Papaverine will also overcome arterial spasm and may benefit the skin in other conditions, e.g., frost-bite, by improving the blood supply and nutrition. The author has found intravenous drips of procaine hydrochloride, 1 g. in saline, repeated for a few days, most useful, or procaine amide can be tried orally.

In a follow-up by Brain and Calnan of 614 patients with haemangiomas treated at the Hospital for Sick Children, radium was used in 48%, x-rays in 16%, both forms of irradiation in 12%, and no treatment in 24%. Ultimate results in treated and untreated patients were equally satisfactory although, in the latter, which probably included the smaller lesions, the process of involution was slower. On the other hand, Andrews *et al.* in New York, after twenty years' experience, recommend early treatment for every angioma. They advise sclerosing solutions for lesions around the eye and x-rays for the lips, but radium is their usual treatment.

A survey of dermatological patients who had had x-ray therapy was made by the New York Skin and Cancer Unit, and their findings were that, in those who had been given total doses of more than 1000 r. some sequelae, mostly cosmetic, occurred. The amount of radium needed to cure cancer of the skin caused mild sequelae in about 20% of patients. Severe injuries from irradiation result from damage by the more penetrating rays to the blood vessels and other deeper tissues. This can be avoided by using softer rays which are sufficiently powerful to treat many of the common skin disorders. Ebbelhøj recommends a half-value layer equal to the thickness of the diseased part. Although more than 90% of the emanation from thorium X is alpha rays with very small penetrating powers, yet Witten and Lazar report that most of the lesions in a patient with multiple benign superficial basal cell epitheliomas responded favourably after two or three courses of thorium X.

The frequency of contact dermatitis after local application of antihistamines was 8%. The replies of 200 dermatologists to a questionnaire by Ellis and Bundick as to whether antihistamines for local application should be taken off the market were 29% for such a measure, 37% against; the others desired some form of restriction.

Liquid nitrogen has been used by Morgan to freeze warts. An application on a swab of cotton wool for 5 to 30 seconds is said to be sufficient. Vilanova and his colleagues found that podophyllotoxin was the most effective constituent of podophyllum resin. Patch tests with a 1/1000 dilution of podophyllotoxin were always negative. They tried to dry up moist eczema and contact dermatitis by applying 1 or 2 parts per thousand of podophyllotoxin in zinc paste which was renewed after 12 hours. Improvement was appreciable after 24 hours. Duthie and McCallum treated plantar warts with podophyllum resin after paring away the horny top and macerating the wart under elastoplast. Belisario used a similar technique but incorporated 50% resin in compound tincture of benzoin. Smith and Garrett used the resin in the same vehicle on superficial epitheliomas. Obstinate patches of lichenification will sometimes respond to applications of podophyllin.

A. C. R.

SPIDER ANGIOMAS APPEARING DURING TREATMENT WITH TRIHEXYPHENIDYL.

C. L. HOLT. (1953) *New Engl. J. Med.*, 249, 318.

Two patients, a man and a woman, while taking trihexyphenidyl for Parkinson's disease, developed enormous numbers of pulsating spider angiomas on the face, neck and chest. These disappeared after withdrawal of the drug which may, it is thought, have been responsible for them.

A. D. P.

EPITHELIOMA ADENOIDES CYSTICUM WITH GLANDULAR METASTASIS. L. TORO

GENKEL. (1953) *Rev. argent. Dermatosis*, 37, 43.

A woman aged 38 had developed about 10 years earlier itchy infiltrated pinkish plaques and also some small papules behind both ears. After a few months of rubbing to relieve the itching the adjacent lymph glands enlarged and had remained so for 3 years. About a year before she came for consultation itchy papules appeared on various parts of the face. Histological sections from the first biopsy were inconclusive, but from a second one over the left mastoid showed hyperplasia of the hair follicles, proliferation of the basal cells, cavitation and epidermal cysts. Sections of an epitrochlear gland had a similar histological picture except that calcification was taking place in some areas, evidence of spontaneous involution. No evidence of a carcinomatous process was seen.

G. W. B.

DERMATOMYOSITIS. A CLINICAL STUDY. J. M. BORDA, J. ABULAFIA and S. G. STRINGER. (1953) *Arch. argent. Dermatol.*, **3**, 175.

DERMATOMYOSITIS. A HISTOLOGICAL STUDY. J. M. BORDA, J. ABULAFIA and S. G. STRINGER. (1953) *Arch. argent. Dermatol.*, **3**, 199.

The first paper gives the clinical findings and course of the disease in 13 patients. The authors regard it as an allergic manifestation with a multiple aetiology, so treatment is guided by the clinical findings.

From histological examination of biopsy specimens the initial change appears to be an alteration in the endothelial lining of blood vessels. Inflammatory changes are relatively less than the intense signs of degenerative changes in the collagen due to oedema. As there is little sign of any recuperative action in the histiofibroblastic elements they probably receive some direct injury. The same can be said of striated muscle which sometimes showed much more severe degenerative changes than did the collagen. The disease is not merely a collagenosis but a mesenchymosis.

G. W. B.

RINGWORM DISEASES IN JAMAICAN SCHOOLCHILDREN. F. W. JACOBSON. (1951) *W. I. med. J.*, **1**, 64.

The types of fungous infection encountered are much the same as in this country. *M. Audouini* is the commonest cause of ringworm of the scalp though trichophyton infections are also common but do not create such an epidemiological problem because of their lower child to child infectivity and because an attack confers immunity. Favus is seen occasionally. Tinea versicolor is extremely common. Secondary infection occurs very readily and over-treatment, especially in acute and eczematized cases, is rightly condemned as being even more disastrous in tropical than in cooler countries.

R. D. S.

THE MODERN TREATMENT OF FRAMBOESIA (YAWS). K. R. HILL. (1951) *W. I. med. J.*, **1**, 81.

In native communities the treatment of yaws must be considered from the point of view of a public health problem, and the only practical and worth while aim is the total eradication of the disease; otherwise latent and missed cases reinfect the population. Arsenicals, bismuth, penicillin, aureomycin and chloramphenicol are compared in efficiency, toxicity, ease of administration and supervision, and cost, and the author concludes that two injections of procaine penicillin G in oil with 2% aluminium monostearate at three to five day intervals is by far the most satisfactory. Aureomycin and chloramphenicol are probably as satisfactory clinically but the cost and the need of supervision for a fortnight while the drugs are taken by mouth make them impracticable for mass campaigns in uneducated populations.

R. D. S.

FRAMBOESIA (YAWS) TREATED WITH AUREOMYCIN. K. R. HILL, K. RHODES, G. S. ESCOFFERY and C. C. MURRAY. (1951) *W. I. med. J.*, **1**, 93.

Ten early cases of yaws cleared completely and remained clear for at least one year after treatment with aureomycin, 25 mg. per kilo body weight, for 14 days. The clinical improvement was rather slower than after penicillin treatment but there was a more regular and more rapid reversal of the Kahn reaction.

R. D. S.

LEPROSY IN JAMAICA. E. L. DE MONTAIGNE. (1953) *W. Ind. med. J.*, **2**, 125.

This paper is mainly a discussion of the sulphones and their use in the treatment of leprosy. In the first few paragraphs, however, the author makes some valuable observations on early signs of the disease which include nodules on the lobes of the ears, a slight contracture of a little finger and, most important, various lesions in the eyes, which may precede any cutaneous manifestations.

R. D. S.

CLASSIFICATION OF LEPROSY. S. N. CHATTERJEE. (1953) *Antiseptic*, **50**, 499.

The Indian journal, *The Antiseptic*, has devoted its July 1953 number to dermatology and leprosy. Most of the articles are simple texts for general practitioners and so of little interest to dermatologists, but in his "Classification of Leprosy," S. N. Chatterjee discusses in some detail the difficult indeterminate and transitional cases that defy any neat system of filing, if only because they will keep jumping from one pigeon hole into another. H. Paul gives an authoritative account of its modern treatment, including the chemistry of the sulphones.

R. D. S.

THE EVERLASTING ECZEMA. A RETROSPECT. J. E. M. WIGLEY. (1953) *Austral. J. Derm.*, 2, 5.

This scientific and philosophical article is more than its title claims: it is also a review of the modern theories concerning eczema, and a statement of some of the problems of present-day research.

Admirably brief, it is likely to help the dermatologist in clarifying his thoughts, and to provide an ample groundwork for a series of lectures to postgraduate students. R. E. B.

OINTMENT BASES. J. S. PEEL. (1953) *Austral. J. Derm.*, 2, 11.

The student of dermatology finds it difficult to collect information on this subject: here is a good article which considers the common ointment bases from the pharmaceutical aspect: physical properties, compatibilities and contraindications are all studied. The author notes that lanoline has been deleted from the U.S.P. on the grounds that it is a sensitizing agent: it would have been of great interest if he could have added some indication of the comparative sensitization rates of the other substances in common use. R. E. B.

TOPICAL PODOPHYLLIN THERAPY WITH SPECIAL REFERENCE TO LICHEN CHRONICUS (SIMPLEX) CIRCUMSCRIPTUS (NEURODERMATITIS CIRCUMSCRIPTUS, LICHEN VIDAL). JOHN C. BELISARIO. (1953) *Austral. J. Derm.*, 2, 18.

Podophyllin in tinct. benz. co. has been used by the author in 80 consecutive cases of lichen simplex, 38 of the suboccipital variety. The results are stated to be most gratifying, all but two of the suboccipital lesions having disappeared. Unfortunately, the series was not controlled, the duration of the follow-up is not stated, and an unspecified number of the patients received tar and menthol as well.

Treatment must be modified from patient to patient on account of the inflammatory reactions sometimes arising, but can be summarized as follows:

1. Clip hair short over affected area.
2. Test a small portion with 5% podophyllin.
3. Continue at weekly intervals, strengthening gradually up to 20% or reducing to 1% or 2% according to the reactions or fortitude of the patient.

The article occupies eight pages and includes 49 references, remarks on the aetiology of lichen simplex, and on podophyllin therapy in general. R. E. B.

THE FRACTURE BLISTER. W. R. BUCKLEY and W. C. LOBITZ. (1953) *New Eng. J. Med.*, 249, 11.

Bullae may develop at the site of injury in fractures produced by direct trauma and with severe soft tissue injury. The bullae may appear as early as 12 hours after trauma or as late as the twenty-fifth day. They may occur in fractures at any site and in patients of either sex and of any age; they are, however, most frequently seen on the leg. Ten cases were studied. The bullae were formed by dermo-epidermal separation, but a single layer of compressed epidermal cells was usually noted on the floor of the bulla. A. J. R.

PROGRESSIVE SYSTEMIC SCLEROSIS (SCLERODERMA). P. M. BEIGELMAN, F. GOLDNER and T. B. BAYLES. (1953) *New Eng. J. Med.*, 249, 45.

The authors, who prefer the term "Progressive Systemic Sclerosis" suggested by Goetz, report 15 new cases. Fourteen of them showed systemic involvement. The electrocardiographic changes were prominent but variable. Arrhythmias were the commonest abnormality. The most frequent x-ray changes were pulmonary, cardiac or oesophageal but soft tissue, bone and joint lesions were also detected. The postmortem findings in the 5 fatal cases are summarized. The authors discuss the relationship of scleroderma to the other collagen diseases and suggest that the essential difference is perhaps in the intensity and diffuseness of the reaction. They consider that there is no satisfactory evidence for establishing acrosclerosis as a distinct entity or even as a special form of scleroderma. A. J. R.

THE CYTOLOGY OF THE EXUDATE IN ECZEMA DISEASES. K. FISCHER. (1953) *Derm. Wschr.*, 128, 768.

In smears from the vesicle content (from the primarily affected areas) in seborrhoeic eczema and contact eczema the author found the average of mononuclear cells to be 73.5% in contact eczema and 24.9% in the other; the mononuclear count from a positive vesicular patch test in

contact eczema was 33.9%. A blood smear from the area of a positive patch test in a contact eczema patient showed no difference from one obtained from apparently normal skin in the same patient or from normal skin in a patient with seborrhoeic eczema. The smear from a cantharides blister in 5 patients with contact eczema showed over 50% mononuclears, the average from 23 patients with seborrhoeic eczema was 34.8% and from 11 controls 25%. In a patient with a pustular contact eczema due to marfanil the mononuclear count was 21.7%. M. S. S.

DIFFUSE HYPERPLASIA OF THE SEBACEOUS GLANDS OF THE FACE IN ANALOGY TO RHINOPHYMA. E. KEINING and O. BRAUN-FALCO. (1953) *Derm. Wschr.*, 127, 463.

The authors regard rhinophyma as a disease entity affecting the male and invariably accompanied by seborrhoea, whereas rosacea is a disease predominantly of the female (2,3) and seborrhoea may be by no means a presenting feature, but hypertension is no unusual accompaniment. Rhinophyma again is frequently present without rosacea. They describe in a woman aged 70 a very unusual diffuse rhinophyma-like involvement of the skin of the whole face, which was very greasy and thickened with coarse pores: histologically, as in rhinophyma, much hyperplasia of sebaceous glands with well marked basement membrane: new vessels, many mast cells and young connective tissue cells and polychromasia of cement substance due to presence of hyaluronic acid (disappearance on treating with hyaluronidase). The acini in their central part contained glycogen (normally absent in ripe cells). She suffered from a general sclerosis, hypertrophy of the left ventricle, and had a scar at the exit of the stomach. Her skin had been excessively greasy from her youth. She showed no evidence of rosacea but had slight bilateral conjunctivitis with patches of superficial keratitis on the left eye. M. S. S.

CORTISONE AND EXPERIMENTAL STREPTOCOCCAL INFECTION IN THE MOUSE. A. LÜTZENKIRKCHEN. (1953) *Derm. Wschr.*, 128, 688.

The conflicting reports on cortisone in infection prompted the author's investigation. Cortisone was injected 2 hours after intraperitoneal infection of white mice with streptococci and was continued for a further 2 days (10 groups of 10 mice were given steadily increasing dilutions of the infecting dose, 10^{-6} to 10^{-20}). All mice in the first four groups were dead by the second day (by the fourth day in the fifth), and still alive in steadily increasing number on the tenth day in the last five groups: thus cortisone in the dosage given did not influence the course of the infection. Increasing the dosage of cortisone increased also the number of mice alive on the third day but the good effect lasted only for the 3 days the cortisone was given: by the tenth day there was no improvement in the treated group as compared with the untreated. The dosage here corresponded to one still tolerable in man: but by increasing it 2 to 4 times (corresponding to a total dose of 1050-2100 mg. in a 70 kg. man) the mortality was increased in both infected and uninfected mice—a toxic cortisone effect. Cortisone in large doses given for three days before infection had no influence on the course of the infection. In the final experiment 10 times the hitherto intraperitoneal infecting dose was injected subcutaneously to produce a local instead of a general infection to test the generalizing factor of cortisone. The number alive at the end of 3 and 10 days showed no difference in the treated and untreated groups, thus the author's experiments yield no evidence that cortisone favours the spread of infection.

M. S. S.

CHANGES IN SALIVARY SECRETION IN SKIN DISEASES. G. W. KÖRTING and W. KLEIN-SCHMIDT. (1953) *Derm. Wschr.*, 128, 772.

The authors have investigated the salivary secretion (collected over a period of 2 hours) in 80 skin patients: the quantity, expressed as minute volume, the percentage concentration of potassium thiocyanate, and chloride, and their absolute excretion as mg. per hour (the diastatic activity and hydrogen ion concentration were estimated but the results were so variable as to be inconclusive).

It was found that with age the minute volume decreased and the concentration of potassium thiocyanate and chloride content increased.

In seborrhoeic eczema (18 patients) there was a diminution of the average minute volume with increased chloride concentration. The hourly excretion of chloride was diminished. In general there was a tendency to reduced salivary function but the potassium thiocyanate excretion was reduced in smokers only.

In endogenous eczema (13 patients) there was a large increase in salivary production but the hourly excretion of potassium thiocyanate and chlorides was diminished.

In psoriasis vulgaris (12 patients) salivation was much increased and the hourly excretion of potassium thiocyanate and chlorides was increased.

The differences in the three disease groups had no relation to age.

M. S. S.

NOSOPARASITIC SKIN DISEASES. M. HORNEMANN. (1953) *Derm. Wschr.*, 128, 685.

The author seeks to discover whether skin diphtheria in its commonest, eczematoid, form has characteristics that might suggest the diagnosis.

In the author's 71 patients the bacilli were almost exclusively of the pseudo or paradiphtheria type and were accompanied by a mixed flora (the *Staphylococcus haemolyticus* or *aureus* predominating). The appearances were mainly those of eczema dermatitis affecting usually the lower leg. He considers that, although primarily saprophytic, the organisms acquire virulence owing to the weakened nature of the terrain and can thus exert their characteristic harmful influence, preventing healing until treated by remedies directed towards the organisms (he recommends compresses of trypanflavine 1-20,000 solution). As the organisms themselves do not give rise to the skin disease but only under the special circumstances described he suggests the term "nosoparasitic skin diphtheria."

M. S. S.

THEORETICAL, EXPERIMENTAL AND CLINICAL STUDIES ON THE ACTION OF NOVOCAIN UPON THE ORGANISM ESPECIALLY THE SKIN. E. HEINE. (1953) *Arch. Derm. Syph., Berl.*, 195, 16.

First the theories in which affections of the nervous system are implicated in the genesis of disease processes generally are reviewed. The action of novocain upon human skin, by injection locally, in ganglion block, or intravenously, was tested by measurement of skin resistance, skin temperature, pH of skin surface and capillary microscopy. A non-specific effect of novocain, mediated by a pituitary-adrenal mechanism, is adduced. Striking clinical results are claimed in leg ulcers, circumscribed scleroderma, neurodermatitis and herpes zoster. Improvement was obtained in hidradenitis and furunculosis, also in diffuse scleroderma, intoxication after burns, pruritus ani and eczema.

M. F.

CHRONIC RELAPSING APHTHOSIS INCLUDING BEHCET'S TRISYMPOM COMPLEX. R. HAENSCH. (1953) *Arch. Derm. Syph., Berl.*, 195, 362.

A microphotograph of a scraping from the buccal mucosa shows elementary bodies of a virus with some resemblance to herpes simplex. Aphthous stomatitis of proven herpetic origin is a separate entity, as is Stevens-Johnson syndrome.

M. F.

RELATIONSHIP OF KLIPPEL-TRENAUNAY-WEBER SYNDROME TO PARTIAL GIGANTISM. F. FEGELE, J. HOLTSCHMIDT and S. KOHRS. (1953) *Arch. Derm. Syph., Berl.*, 195, 402.

Twelve cases collected in the Hamburg clinic in a relatively short time suggest that the condition is not so rare. It is not the result of a genetic defect or mutation but of injury to the vegetative nervous system at an early stage of development. Perhaps partial angiectatic gigantism is a good name.

M. F.

CLINICAL OBSERVATIONS ON DERMATOSES TREATED WITH CORTISONE OR ACTH. A. LUETZENKIRCHEN. (1953) *Arch. Derm. Syph., Berl.*, 195, 459.

Results from the Cologne clinic are tabulated; a series of 63 patients. At the moment in the United Kingdom the supply position is difficult and the dermatologist must content himself with trying to secure the drugs for patients who would die without them. When more drugs are available, it would seem that some difficult decisions await the dermatologist.

M. F.

LIPOATROPHIA ANNULARIS. A CASE OF A YET UNDESCRIBED DISEASE OF THE SKIN (OF THE PANNICULUS ADIPOSUS). J. FERREIRA-MARQUES. (1953) *Arch. Derm. Syph., Berl.*, 195, 479.

A band of fat atrophy encircled the left forearm of a 40-year-old woman. Photographs and histology.

M. F.

HAIR LOSS FROM SEBUM. PETER FLESCH. (1953) *Arch. Derm. Syph., Chicago*, 67, 1.

Experiments on laboratory animals with human sebum and 3 of its constituents, squalene, oleic acid and linoleic acid showed that local application caused reversible baldness with acanthosis and hyperkeratosis. There are probably other unsaturated fatty acids in sebum which have a depilatory action. The effect is related to the presence of $\text{—C}=\text{C—}$ groups, and appears to be due to interference with sulphhydryl groups. It is possible that sebum may influence hair growth and keratinization in man. J. K.

DIAGNOSTIC PITFALLS OF DERMAL PATHOLOGY. MARCUS RAYNER CARO. (1953) *Arch. Derm. Syph., Chicago*, 67, 18.

This excellent article is worth the attention of all dermatologists, and is especially valuable to those starting the exploration of the badly charted seas of this branch of medicine. The great importance of combining clinical and histopathological knowledge and experience in reaching a diagnosis in difficult cases is rightly stressed. J. K.

USE OF DIMERCAPTOL (BAL) OINTMENT IN CHRONIC CHROME DERMATITIS. H. N. COLE, Jr. (1953) *Arch. Derm. Syph., Chicago*, 67, 30.

Dimercaptol, 3% in ointment, was effective in treating experimentally produced chrome dermatitis in animals and in 7 cases of the disease in men. Intolerance was shown in one case. J. K.

SANDPAPER ABRASION OF TATTOOS. ERNEST A. STRAKOSCH. (1953) *Arch. Derm. Syph., Chicago*, 67, 53.

Three college students were tattooed on Saturday night and repented of it on Monday morning. Fortunately an excellent cosmetic result was got by abrading the areas with sandpaper under a local anaesthetic. J. K.

HYPERSENSITIVITY TO "PARA GROUP." GEORGE RAJKA. (1952) *Acta allergol.*, 5, 11.

The connection between chemical structure and sensitization was demonstrated in 23 subjects who gave positive skin tests to members of the "para group." Nearly all patients showed some cross sensitivity but there was much individual variation in response. H. T. H. W.

PITYROSPORUM OVALE AND SOME SCALY CONDITIONS OF THE SCALP. F. A. WHITLOCK. (1953) *Brit. med. J.*, 1, 484.

Examination was made of 200 normal scalps, and the degree of infection with *P. ovale* was correlated with the degree of dandruff present. It was concluded that there was no evidence to justify the theory that *P. ovale* caused the dandruff. Instead, it was suggested that the degree of infection was influenced by the quantity of sebaceous secretion, and that the increased flow of sebum at puberty would explain the rise in the incidence of infection at that age. It was also noted that the amount of dandruff was heavier in the female.

The suggestion that sebaceous secretion was the main factor influencing the degree of infection with *P. ovale* was supported by the findings in scrapings taken from the skin of the nose when compared with scrapings from eyelids in 20 cases. Further support was given by the findings in nine cases of tinea amiantacea, 17 cases of psoriasis of the scalp, and 16 cases of seborrhoeic eczema of the scalp and trunk. In most of these dry scaly conditions the organism was absent or was found only in small numbers.

The suggestion that oestrogens diminish the degree of dandruff and *P. ovale* infection receives no support from the findings in the 100 male and 100 female normal scalp scrapings.

It is concluded that *P. ovale* is not the cause of dandruff, but is a harmless organism on the scalp which thrives best in the medium provided by a heavy flow of sebum. B. A. T.

SKIN LESIONS IN ORGANIC BRAIN DISEASE. E. E. ROBERTSON. (1953) *Brit. med. J.*, 1, 291.

Attention is drawn to earlier descriptions of bullous eruptions occurring in epidemic encephalitis and as a sequel of prefrontal leucotomy. Cases are here described in which cerebral tumour, carbon monoxide poisoning and subdural haematoma were associated with cutaneous bullae, indicating that varying types of cerebral pathology can produce the same cutaneous lesion. A fourth case described the association of a subdural haematoma with dermatitis. B. A. T.

HUMAN MELANOGENESIS—THE TYROSINASE REACTION IN PIGMENT CELL NEOPLASMS, WITH PARTICULAR REFERENCE TO THE MALIGNANT MELANOMA—PRELIMINARY REPORT. THOMAS B. FITZPATRICK. (1952) *Arch. Derm. Syph., Chicago*, **65**, 379.

Tyrosinase activity was investigated histochemically and biochemically in specimens of normal skin, pigmented naevi and melanomas; the effect of added tyrosin was estimated by presence or absence of melanin formation in the melanogenocytes (an up-to-the-minute name for melanoblasts) and by measurement of oxygen uptake.

The following conclusions were reached: An inhibited tyrosinase system occurs in unirradiated skin, but an active one in skin irradiated *in vivo* with ultra-violet light; a partially inhibited tyrosinase system appears to exist in actively proliferating junction naevi; an active tyrosinase system occurs in melanotic and amelanotic melanomas. Experiments on other neoplasms showed no tyrosinase activity. Sulphydryl inhibitors failed to remove the inhibition of tyrosinase in normal skin.

The tyrosinase reaction may help in the diagnosis of malignancy in pigment-cell neoplasms, and in the diagnosis of amelanotic melanoma from other undifferentiated malignant lesions which it simulates.

It is hoped, in future experiments, to be able to evaluate new formation of melanin in cells in which it is already present by adding a radio-active tracer to the tyrosine used. J. K.

STRESS STUDIES IN THE ECZEMA-ASTHMA-HAY-FEVER DIATHESIS. THOMAS H. STERNBERG and MURRAY C. ZIMMERMAN. (1952) *Arch. Derm. Syph., Chicago*, **65**, 392.

Eosinophil counts were carried out on 27 patients suffering from "atopic dermatitis" most of whom had also personal or family histories of allergy, and on 22 controls. Normally there was no significant difference between the two groups, nor in the amount of eosinopenia after injection of epinephrine, but after one hour's exposure in a hot room (100–115°F. and 85–95% humidity) the controls showed a similar reduction of eosinophils but the patients little or none.

The authors conclude that patients with atopic dermatitis have an intact and properly functioning pituitary-adrenocortical mechanism and infer that the cause of their abnormal response to the stress is in the higher brain centres or in the adrenal medulla. J. K.

PITUITARY ADRENOCORTICOTROPIC HORMONE (ACTH) AND CORTISONE IN DISEASES OF THE SKIN—II. ALLERGIC AND OTHER DERMATOSES. REPORT OF 67 CASES. J. GARDNER HOPKINS, BEATRICE M. KESTEN, CARL T. NELSON, GEORGE W. HAMBRICK, JR., ROYAL G. JENNINGS and GERALD F. MACHACEK. (1952) *Arch. Derm. Syph., Chicago*, **65**, 401.

The first part of this report, by a different set of authors, dealing with pemphigus and other bullous dermatoses, appeared in *J. amer. med. Ass.*, **145**, 201 (1951). The present report shows benefit from this treatment in drug eruptions, urticaria (all cases except one were of short duration and all not due to light) and dermatitis venenata; temporary benefit in lupus erythematosus, lichen planus, dermatitis herpetiformis, chronic dermatitis of unknown cause, leukaemia cutis, mycosis fungoides and allergic eczema; probably no benefit in dermatomyositis, arthropathic psoriasis, Sjögren's syndrome, solar urticaria, Kaposi's sarcoma, acanthosis nigricans, nodular non-suppurative panniculitis and alopecia totalis. Complications were noted in 27 patients; all were temporary, though one patient in a state of depression attempted to commit suicide.

J. K.

ACUTE FORMS OF PEMPHIGUS. H. E. MICHELSON. (1952) *Arch. Derm. Syph., Chicago* **65**, 422. **CHRONIC PEMPHIGUS VULGARIS.** FRANCIS E. SENEAR. (1952) *Arch. Derm. Syph., Chicago*, **65**, 429.

These two articles are complementary. The first, after excluding the rare acute ("butchers") pemphigus, discusses the difficulty in differentiating acute from chronic pemphigus vulgaris. The course of the disease appears to be the chief criterion. The possible insidious onset of pemphigus with nondescript eruptions is stressed. Biopsies were done in all cases of pemphigus, but the author considers that pemphigus cannot be diagnosed microscopically, and agrees that interpretation of the Tzanck test is, "except perhaps in very skilled hands, a ticklish affair."

The second article is a brief review of recent ideas on the cause, diagnosis, histopathology and treatment of chronic pemphigus vulgaris. The author agrees that it is difficult to distinguish between the acute and chronic forms of the disease as recognized in U.S.A. He points out the frequency with which cases vary from time to time in their clinical manifestations, not only from

one form to another of pemphigus but from pemphigus to dermatitis herpetiformis and *vice versa*. The different views on the histopathology of the group are given and the conclusion reached that "often continued observation over a variable but often prolonged period may make a diagnosis possible." J. K.

ANOMALIES OF PIGMENTATION. G. B. DOWLING and F. A. WHITLOCK. (1952) *Practitioner*, 168, 453.

A valuable summary of our present knowledge of melanogenesis, developmental anomalies of pigmentation, disturbances of pigmentation in systemic disease, war melanoses, avitaminoses, hormonal disturbances and diseases of the skin.

There now seems to be fair agreement that there is in the skin a copper-containing enzyme now known as tyrosinase (= dopa oxidase) which is able to convert tyrosine to dopa and dopa to melanin. The activity of tyrosinase is inhibited by aminoacids containing sulphhydryl groups, especially glutathione. This restraining activity of sulphhydryl is abolished by metals such as iron, copper and arsenic, so that the pigmentation following arsenical treatment is explained. Thiourea and thiouracil inhibit tyrosinase *in vitro*, and Hellerstein describes a negro who developed patches of depigmentation while under treatment with thiouracil. Ascorbic acid as well as sulphhydryls may inhibit melanin formation.

Hair pigments behave differently from skin pigments, and the facts about tyrosinase and its inhibitors described above do not apply to hair. The pigmentation following radiation appears to be due to destruction or oxidation of the sulphhydryls and perhaps the ascorbic acid in the skin. Reduced melanin can be oxidized to a darker melanin immediately by the visible rays of the spectrum.

It is possible that the pigmentation of Addison's disease is due to the increased activity of tyrosinase in the lowered sodium chloride concentrations which occur in Addison's disease.

Albinism is a recessive character resulting in the absence of melanoblasts from the skin. Consequently, as it is these cells which contain the tyrosinase, no melanin can be formed.

Vitiligo appears to be due to absence or exhaustion of the skin tyrosinase.

A. C. R.

KELOIDS AND THEIR TREATMENT. BETHEL SOLOMONS, Jnr. (1952) *Practitioner*, 168, 465.

Both local and general factors are necessary for the production of keloids. In the cicatricial type Glucksmann has shown that various particles, such as cotton-wool fibres or talcum powder, act as foreign bodies to provide the local factors necessary for their evolution. Hereditary and familial influences may play a small part. Keloids should be treated as soon as their growth is recognized, for which radiotherapy produces the best results. Prophylactic treatment by this means can be effective. Preliminary investigations with ACTH and allied substances suggest that they may yet play a part in the treatment and elucidation of the general systemic aspect of this disease.

A. C. R.

CHROMATIN-MELANIN RELATIONSHIPS IN MALIGNANT MELANOMATA. E. MEIROWSKY and L. W. FREEMAN. (1951) *J. invest. Derm.*, 16, 257.

An attempt is made to convince the reader that melanin is produced, not in the melanoblast or other element of the mesenchyme, but in the epithelial cell alone. It is also proposed that its precursor is nucleic acid, and that the reaction producing it takes place on the surface of the nucleus or in a nucleolus. The argument appears to consist of little more than repeated statements that the nucleus is the main centre of metabolic activity in the cell and that melanin is abundant in its neighbourhood.

J. H. T. D.

COMPARATIVE STUDIES ON THE EFFECT OF ANTI-CHOLINERGIC COMPOUNDS ON SWEATING. W. B. SHELLEY and P. N. HORVATH. (1951) *J. invest. Derm.*, 16, 267.

Suppression of sweating can be obtained by ingestion of atropine 3 mg. (1/20th gr.), a dose sufficient in most people to produce uncomfortable side-effects; 16 other anticholinergic drugs administered in customary dosage had no effect.

After a preliminary experiment in which the drugs in aqueous solution were introduced into the skin by iontophoresis, a more extended trial of laevorotatory hyoscine hydrobromide showed that, in sufficient concentration, an aqueous solution applied to the skin could produce lasting anidrosis. For example, an 18% solution applied for 10 minutes to a field of 6 sq. cm. produced anidrosis over an area of 70 sq. cm. lasting nearly a month.

J. H. T. D.